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Among 653 children with Hodgkin's disease who underwent treatment from 1971 to 1993, 44 pts (6.7%) were diagnosed with stage IV disease. The treatment consisted of MVPP (mechlorethamine, vinblastine, procarbazine, prednisone) alone or alternatively with B-DOPA (bleomycine, dacarbazine, vincristne, prednisone, doxorubicin), combined with involved field radiotherapy (IF-RT) in 38 pts. Follow-up was completed on December 31, 1996. The therapeutic results of the stage IV pts were compared in the three periods when the therapy was modified:

I. 1971-82, n=12 - all pts received MVPP, in 7 pts chemotherapy (CT) was combined with IF-RT (30-45Gy),
II. 1983-87, n=14 - all pts received MVPP/B-DOPA, in 13 pts CT was combined with IF-RT(30-45Gy),
III. 1988-93, n=18 - all children received MVPP/B-DOPA combined with low dose IF-RT (20-30Gy).

In these periods, the first complete remission was achieved in 67%, 86% and 83% of children, respectively. The 8-year disease free survival was 62%, 87% and 100%, respectively, and the 8-year event free survival was 42%, 64% and 83%, respectively. Toxicity of therapy was reasonable. Secondary malignancies were not observed within the follow-up period.
Multi-drug chemotherapy combined with low dose IF-RT might cure more than 80% children with stage IV Hodgkin's disease and it currently seems to be an optimal method of treatment.

P-182

HIGH INCIDENCE OF CENTRAL NERVOUS SYSTEM RELAPSES IN NON-IRRADIATED CHILDREN WITH T-ALL. RESULTS OF FRALLE 87 AND FRALLE 89 STUDIES.

Leblanc T, Auclerc MF, Landman-Parker J, Cornu G, Stephan JL, Debré M, Lejars O, Edan C, De Lumley L, Perel Y, Couillault G, Sommelet D, Baruchel A, Leverger G and Schaison G. Hôpital Saint-Louis, Paris, FRANCE for the FRALLE group.

PATIENTS: From june 87 to december 91, 952 consecutive children with newly diagnosed ALL were included in FRALLE 87-89 studies. 136 pts were included in the mediastinal group and among them immunophenotypic studies assessing a T-cell phenotype were available in 128 pts (94%). Out of them, 19 pts had less than 25% bone marrow blasts and are excluded from this analysis. The 109 remaining pts are herein analysed. TREATMENT SCHEDULE : treatment associated a 5-drug induction, 4 courses of consolidation with HD-MTX (87: 3g/m², 89: 8g/m²), 12 multidrug reinductions and 1 yr of maintenance. The cumulative dose of DNR was 480 mg/m². Folinic acid rescue (12 injections) was not monitored in these trials. CNS prophylaxis comprised 12 triple during the first 18 months. RESULTS : D20 bone marrow is evaluable in 105 pts. 94 pts had < 5% blasts. 8 had 5-24% blasts: all of them reached CR. 3 had < 25% blasts and received a second course with vincristin and steroids ; 2 reached CR. Only 4 pts did not reach CR (1 toxic death, 3 leukemic failures). The overal CR rate is 96,3%. There are no statistical difference for the distribution of presenting features in the 2 protocols. The EFS for FRALLE 87 and 89 are respectively 31±14 and 44±11% (NS). The EFS and Survival for both protocols are respectively 35±10 and 48±10%. In univariate analysis the features significantly associated with a poor outcome are: WBC>100,000): p=0.008, platelets<100,000: p=0.02, lack of CD10 expression: p=0.03 and lack of tumor burden (defined as a large hepatomegaly, splenomegaly or adenomegaly): p=0.05. Relapses occured in 57 children as follows :

Type of relapse	87 (n=35)	median delay	89 (n=74)	median delay
BM isolated	8	13m (2-81)	14	9m (4-50)
BM combined	7	12m (2-27)	5	19m (4-39)
CNS	4	16m (2-40)	16	13m (2-40)
Testis/mediastinum	1/0		1/1	

CONCLUSIONS : 1) The overall CR rate is very good but this does not translate in a good long term outcome in these heavily treated pts, 2) the most striking result is the very high incidence of CNS-relapses (18%) in spite of a CNS prophylaxis which associated HD-MTX and triple IT, 3) in FRALLE 93, 112 pts with T-ALL have been included and skull irradiation (18 Gy) is now mandatory in these pts. With a median follow-up of 21 months only 5 pts have relapsed in the CNS (4%).

P-183

TREATMENT OF CHILDREN WITH B-NHL ACCORDING TO A MODIFIED BFM-90 PROTOCOL IN ANKARA

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The objective of this study is to evaluate the results of the therapy of the modified B-NHL BFM-90 protocol used in our clinic.

From January 1991 to December 1995, 32 newly diagnosed children with B-NHL (26 boys, 6 girls) aged 3-13 (median 6 years) were treated with a modified B-NHL BFM-90 protocol. The main modifications of the original BFM-90 protocol are: 1. MTX dosage was reduced from 5g to 1g/m2 (24 hour infusion) and citrovorum factor therapy was modified, 2. Instead of VM26 we used VP 16 in the same dosage. The Murphy classification was used for staging. Kaplan- Meier method was used to calculate the overall and event free survivals.

There were 4 patients in stage II, 16 in stage III, and 12 in stage IV. In 21 patients the primary tumor was in abdomen, in 5 at the head and neck region and the remaining 6 patients had disseminated disease. Complete remission was achieved at the end of first CC block in 29/32 patients (90.6%)(23 at the end of the first BB block). One patient had tumor lysis syndrome in the first 48 hours of admission and the remaining two had progressif disease and all died.The 3-year overall survival for all patients 81 % and event-free survival was 76.9% . According to the stages, the 3-year overall survival and event-free survival were as follows: In stage III 93.75% and 86.54%; in stage IV 58.3% and 54.69% respectively, in stage II all patients are alive.

This modified protocol showed tolerable toxicity and it is highly suggestive for the patients in stage II and III, however same implication is not valued for the patients in stage IV.

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LARGE CELL ANAPLASTIC LYMPHOMA (ALCL) - THE UK EXPERIENCE

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Objective: To establish the outcome in paediatric ALCL patients treated with the B cell UK 9002 protocol.
Methods: A retrospective analysis of data returns from children with ALCL treated on UKCCSG NHL trial regimens.
Summary: 50 children with ALCL were treated between July 1990 and July 1996. In all cases there was central pathology review. 41/50 (82%) of the children were treated according to the UKCCSG B cell 9002 protocol. Within this group, the male to female ratio was 1.8:1, the age range 2-16 yrs with a median age of 13 yrs. The majority 36 (88%) were Murphy stage 111 at presentation, 5

(12%) stage 11. Nodal involvement was found in 40 (97%) and extranodal disease in 26 (63%). These included 10 (24%) in skin, 7 (17%) in bone and 6 (14%) in lung. 17 (41%) had evidence of B symptoms. The event free survival was 58% with an overall survival of 66%. The median follow up was 45 months (range 12-77). 17 patients relapsed - 7 on treatment and 10 off treatment (range 1-20 months, median 3 months). Of the relapsed patients only 3/17 (18%) survived following further therapy, 2 in 2nd CR (17, 26 months respectively) and 1 is alive with stable disease, 11 months after a second relapse.

Conclusion: The overall survival of this group of patients was 66%. Patients tended to relapse early and response to second line therapy was disappointing. Novel treatment strategies e.g. Vinblastine based, are needed, but require large patient numbers within a cooperative study.

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HODGKIN'S DISEASE IN CHILDREN ; OUR EXPERIENCE IN 46 CHILDREN IN GAZİ UNIVERSITY.

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Our aim is to evaluate the characteristics and the combined modality treatment results of Hodgkin's disease in our center in Turkey.

From January 1991 to December 1995, 46 newly diagnosed children with Hodgkin's disease were seen. Ann-Arbor classification was used for the staging. All patients were staged clinically (staging laparotomy wasn't done in any of the patients). Patients in stage I and II were treated with three cycles of COPP or ABVD + low dose involved field radiotherapy ; in stage III three cycles of COPP +low dose involved field radiotherapy + three cycles of COPP, in stage IV six cycles of COPP/ABVD altemate therapy + low dose involved field radiotherapy. Kaplan-Meier method was used to calculate overall and event-free survivals.

Out of 46 patients ,38 (82.6%) were male, 8 (17.4%) were female.Median age was 7 (range 1.8 and 14 years), 69.6 % of the patients were under 10 years of age. There were 8 patients in stage I, 17 in stage II, 17 in stage III, 4 in stage IV. Fifteen patients presented with B symptoms(32.6%). Histological patterns were classified as follows: 18(39.1%) mixed cellularity, 15 (32.6%) nodular sclerosis, 9 (19.6%) lymphocyte predominant, 4 (8.7%) lymphocyte depletion. The 3-year overall survival for all patients was 89% , event-free survival was 85% . According to the stages, 3- year overall and event-free survival were as follows: In stage I-II 100%, 96%; in stage III-IV 77%, 71.7% respectively.

Our data showed that unlike developed countries early onset, male gender and mixed cellularity predominancy was seen in our patients. Our treatment results were comparable with the good results of the literature.

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PERIPHERAL T-CELL LYMPHOMA IN CHILDREN AND ADOLESCENTS: A REPORT OF THE BFM-GROUP

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We investigated the clinical characteristics and treatment outcome of peripheral T-cell lymphoma (PTCL) in the three consecutive multicenter studies on non-Hodgkin lymphomas (NHL) of childhood and adolescence NHL-BFM 86, 90, 95. Anaplastic large cell lymphoma of T-cell type and lymphohistiocytic lymphoma are considered to be distinct entities, and are therefore not included in the analysis of PTCL. From 10/86 to 12/96 1364 children suffering from NHL of any type were enrolled into these studies from 83 clinics of Austria, Germany, and Switzerland. In 34 cases (2.5 %) a PTCL was diagnosed. The median age was 8.3 years (yrs) (range 0.6-17.1), the male:female ratio 20:14. Stage (St. Jude) was I in 10, II in 7, III in 12 and IV in 5 patients (pts). Seven pts had mediastinal enlargement (2 with mediastinal lymph nodes, 2 with a thymus tumor and 3 with mediastinal enlargement of undefined origin), 2 pts had nodal disease only. Eighteen pts had extranodal manifestation. Sites of extranodal disease were: soft tissue (10), skin (8), lung (2), bone (3) bone marrow (BM) (5), CNS (0). Three pts with complete tumor resection received no chemotherapy and are without evidence of disease for 11, 13 and 28 months (mts). Twenty-eight pts were treated according to the protocol for lymphoblastic lymphoma, 1 according to the B-cell protocol and 2 pts received mixed therapy. The median follow-up was 2.1 yrs (range 1 month -7.4 yrs). pEFS at 5 years is 0.42 (SE 0.12). Twelve pts suffered from tumor failure with a median time of 3.1 yrs (range 0.75-5.2) after first diagnosis. Sites of failure were initial sites in 8 pts (3 with BM involvement had also BM relapse), and initial plus new sites in 2 pts. We conclude: PTCL account for approximately 2.5 % of NHL of childhood; extranodal disease is frequent; the period of risk for relapses is unusual long compared to other subentities.

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The use of 'FLAG' (Fludarabine, High Dose Cytosine and GCSF) in Refractory and Relapsed acute Leukaemia in Children

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Objectives:
To assess the efficacy of 'FLAG' in treating refractory and relapsed AML and ALL in children. To assess its tolerability in a group of children who have previously received multiagent chemotherapy.

Methods:
Retrospective review of 20 children who received 'FLAG' as remission induction regimen following disease refractoriness or relapse. These patients attended the Paediatric Oncology units of The Bristol Children's Hospital and Great Ormond Street Hospital for Sick Children, London.

Results:
20 patients were involved in the study. 14 male; 6 Female. Median age 77 months (Range 4-168). AML in 13 cases; ALL in 4; Biphenotypic in 3. 8/20 had refractory disease; 6/20 were in 1st relapse; 4/20 were in 2nd relapse; 1/20 in 3rd relapse; 1/20 received FLAG as the primary therapy. 12 Patients had relapsed <12 months after the initial diagnosis. CR obtained in 13 patients; PR obtained in 3 patients; 3 patients were considered non-responders; 1 patient is awaiting bone marrow recovery following FLAG. All patients developed Grade 4 Haematological toxicity (Common toxicity Criteria), otherwise the therapy was well tolerated in all patients. 13 patients were BMT recipients post FLAG (7 unrelated donor transplants; 6 sibling allografts). 10 patients are alive 11.7 months post FLAG therapy (range 1 - 18 months); 2 of these have relapsed. 10 patients have died either from progressive disease or transplant related causes.

Conclusions:
FLAG is an effective protocol for inducing remission in refractory or relapsed acute myeloid and lymphoblastic leukaemia in children. It is well tolerated in a group of patients previously treated with intensive chemotherapy and in particular, avoids the further use of anthracyclines. It has an effective immunosuppressant effect for those undergoing further consolidation therapy in the form of BMT.

P-188

A REDUCTION IN THERAPY INTENSITY MAY IMPROVE OUTCOME IN CHILDHOOD AML

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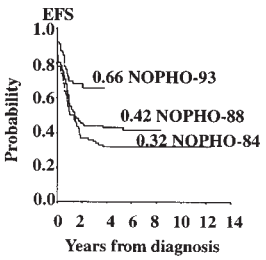

Since July 1984, the NOPHO group has conducted 3 consecutive studies on therapy of childhood AML: NOPHO-84 (n=105) had three blocks of induction followed by four courses of high-dose Ara-C as consolidation, NOPHO-88 (n=118) was an intensification of NOPHO-84 through the addition of VP16 and mitoxantrone to the basic components of NOPHO-84. In addition, in order to increase "upfront loading", the two initial induction blocks should be given close together. This was a highly effective antileukemia protocol, but toxicity was unacceptable and prevented an improved survival (pEFS 0.32 versus 0.42, p=0.2 Br.J.Haematol. 1996;94:82-88).

The protocol NOPHO-93 continued the elements of NOPHO-88, but allowed time for recovery after the first induction block. This made it possible to distinguish between children entering complete remission (CR) after one block and those children having a non-responsive disease requiring an intensified induction approach. 104 children have so far entered the study, 71 of whom obtained a CR after the first block, while 25 children required additional therapy (CR rate 92%). pEFS of all 104 children is 0.66 at 4 years which is a significant improvement from our previous studies (p<0.01, Fig.). For the children going into CR after first block only, the pEFS is 0.81.

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TREATMENT OF CHILDHOOD NON-HODGKIN LYMPHOMA (NHL) IN ARGENTINA. THE GATLA/GLATHEM EXPERIENCE OF 30 YEARS.

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SURVIVAL AND EFS RATES FROM NHL IN CHILDREN HAVE PROGRESSIVELY INCRESEAD OVER THE PAST DECADES DUE TO MULTI-DISCIPLINARY STRATEGIES AND CONTINUAL REFINEMENT OF TREATMENT WIDELY REPORTED IN THE LITERATURE.
THE AIM OF THIS PRESENTATION IS A RETROSPECTIVE REVIEW OF THE RESULTS FROM FIVE CONSECUTIVE TRIALS FOR THE TREATMENT OF NHL CARRIED OUT BY THE SAME COOPERATIVE GROUP.(GATLA / GLATHEM GRUPO ARGENTINO TRATAMIENTO LEUCEMIA AGUDA)
MATERIAL AND METHODS : THE FIRST GROUP (1966-1972) WAS EXCLUDED BECAUSE THE PATIENTS (PTS) DID NOT RECEIVED AN UNIFORM TREATMENT.
FROM 1973 TO 1994, 491 EVALUABLE, PREVIOUSLY UNTREATED NHL PTS < 16 YRS OF AGE WERE ENROLLED: MAJOR CHARACTERISTICS ARE SHOWN IN TABLE 1.

PROT	# PTS	SEX (F / M)	AGE (YEARS) (MEDIAN-RANGE)		B-ALL	MURPHY'S STAGING I	II	III	IV	SITE OF PRIMARY MEDIAST./	ABD
NHL-73	48	21/27	6.5	(1-13)	-	1	6	35	6	13	28
NHL-76	73	24/49	6	(0-15)	-	1	18	47	7	20	47
NHL-81	58	21/37	7	(0-15)	-	2	13	42	1	13	34
NHL-84	145	49/96	5	(1-15)	-	11	28	93	13	21	94
NHL-88	167	35/132	7	(0-15)	17	11	23	96	20	35	97

PROTOCOL NHL-1973 CONSISTING OF (VCR-PRED + SURG. AND/OR RT AS INDUCTION TREATMENT.CRANIOCERVICAL RT+IT MTX-PRED AS CNS PREVENTION.TREATMENT.ANTI-LEUKEMIA (6MP+MTX,VCR-PRED PULSES) OR ANTI-LYMPHOMA (COPP) AS MAINTENANCE, IN A RANDOMIZED TRIAL. NHL-1976: THIS CONSECUTIVE STUDY ADDED DOXO+CFM IN INDUCTION REGIMEN.CNS PREVENTION. WAS PERFORMED WITH 5 DOSIS OF IT MTX - DMT (IDENTICAL MAINTENANCE THERAPY).NHL-1981 SAME INDUCTION REGIMEN,WITH A SECOND LOOK (ABDOMINAL.STAGE III) AS INTENSIFICATION. MTX+6MP + ALT.CYCLES (VCR+CFM+PRED)/(VCR+DOXO+PRED)AS MAINTENANCE
SINCE NHL-1984 THE LYMPHOMAS WERE CLASSIFIED. INTO B OR T -CELL TYPE WITH THE INCORPORATION OF REGIMENS SIMILAR TO BFM-PROTOCOLS. THE LAST TRIAL NIIL-94 WAS OPENED IN SEPTEMBER1994, SO IT LACKS OF ADECUATE FOLLOW UP FOR EVALUATION.

RESULTS CONCERNING DIFFERENT PROTOCOLS ARE AS FOLLOWS IN TABLE 2.

RESPONSE IN CHILDREN WITH NHL ACCORDING TO PROTOCOL							
PROTOCOL	# PTS	# CR (%)	PR	# NU	# DOI (%)	* EFS %	* SV % * (UP TO 60 MONTHS)
NHL - 73	48	21 (43.8)	14	8	5 (10.4)	15	21
NHL - 76	73	64 (87.7)	4	5	0 (0.)	46	47
NHL - 81	58	41 (70.7)	3	4	10 (17.)	42	44
NHL - 84	145	117 (80.7)	7	5	16 (11.)	59	62
NHL - 88	167	150 (89.8)	6	1	10 (5.9)	68	72
p VALUE						p < 0.001	p < 0.001

CONCLUSION: IF WE CONCENTRATE ON THE TWO ENDPOINTS IN THE REVIEW OF THE TRIALS THERE IS A SIGNIFICANT IMPROVEMENT IN OUR THERAPEUTIC RESULTS DURING THE YEARS; HOWEVER WE STILL NEED TO INCREASE OUR EFFORTS IN ORDER TO OPTIMIZE SUPPORTIVE CARE TO AMILIORATE THE INCIDENCE OF DEATH ON INDUCTION

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A PILOT STUDY FOR TREATMENT OF ADVANCED STAGE LARGE CELL NON-HODGKIN'S LYMPHOMA USING INTERMEDIATE DOSE MTX(ID MTX)/HDARA-C. A PEDIATRIC ONCOLOGY GROUP (POG) STUDY

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The overall survival of children with advanced stage large cell NHL has improved to 70%. POG designed a pilot study incorporating ID MTX/HDARA-C to our previous best regimen with the intent to improve EFS.
PATIENTS AND METHODS: Between September 1993 and December of 1994, a total of 28 eligible patients with advanced stage large cell lymphoma (20 stage III and 8 stage IV) were registered. 26/28 patients had central review of the pathology which was 13 immunoblastic, 11 large cell, 2 mixed (lymphocytic-histiocytic). Immunophenotyping was available on 11 patients - 4 were B-cell, 7 were CD 30 positive (4 T-cell and 3 Null-cell). There were 11 males and 17 females, median age at presentation 11 yrs (2-19), and median LDH 569 (143-1549). No patient had CNS disease. Treatment consisted of induction - Vincristine, Prednisone and Doxorubicin (APO). At the end of induction, patients in CR were treated with APO (VCR/6-MP/ADR/Pred) + 8 courses of ID MTX/HDARA-C with G-CSF rescue. CNS prophylaxis consisted of intrathecal MTX. MTX was substituted for doxorubicin after a cumulative dose of 300 mg/m^2 was reached. The total duration of therapy was 12 months.
RESULTS: 27/28 patients achieved CR(20CR,7 provisional CR) and one had progressive disease. 6 patients have relapsed, for an EFS at 2 years of 74.3%(SE11.4). The patient with progressive disease and 5/6 patients who relapsed had the CD30 positive non B phenotype. 6/7 provisional CR are in CCR. The most common toxicity of this protocol was myelosuppression grade 3/4 in 17/27 patients (62.9 %).
CONCLUSION: The addition of ID MTX/ARA-C to APO backbone resulted in a tolerable regimen with acceptable toxicity. Our data showed that the majority of the relapses/progressive disease occurred in patients with CD30 positive immunophenotype. POG is currently evaluating whether ID MTX/HDARA-C combination leads to an increase in EFS and assess the prognostic significance of different immunophenotypes in a randomized study.

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OUTCOME OF CENTRAL NERVOUS SYSTEM (CNS) DISEASE AT DIAGNOSIS OF SMALL NON-CLEAVED CELL LYMPHOMA (SNCCL) IS DEPENDENT ON MARROW STATUS

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Between 1977 and 1995, CCG conducted a series of 5 clinical trials in SNCCL. 46 of a total of 653 patients (pts) (7%) had CNS disease at diagnosis, confirmed on central review. 3 pts were excluded from the CNS disease group based on extradural/clinical spinal cord compression only. The impact of initial CNS involvement upon outcome and pattern of failure in this patient group was examined.

The median age was 9.3 years (yrs) (range 0.8 to 18.7 yrs) and 91% were males. CNS disease included meningeal disease ± CNS parenchymal masses ± cranial neuropathies ("CNS+") in 35 pts, and isolated cranial neuropathies (CNP) in 11 pts. Bone marrow (BM) status was < 5% lymphoblasts (M1) in 19 pts and 5-25% (M2) or >25% (M3) in 27 pts. CNS irradiation was documented in 29/41 pts (71%). Relapse occurred in 19/46 pts (41%). Initial sites of relapse in 14 pts with M2-M3 marrow were: isolated CNS=3, CNS+BM=3, CNS+orbit/abdomen=2, BM+/- other non-CNS=4, isolated testis=2; and in 5 pts with M1 marrow were: isolated CNS=2 and BM+CNS=3. Thus, CNS relapse was a component of initial failure in 13/19=68% of relapses. The event-free survival (EFS) at 3 yrs for 11 pts with isolated CNP of 64 ± 15% was no worse than that of 58 ± 2.4% for 421 pts with disseminated SNCCL without CNS involvement. The 3-yr EFS for 13 pts with "CNS+" and M1 marrow was 54± 14% compared with 64± 2.7% for 331 pts with M1 marrow without "CNS+" disease (p=N.S.). The 3-yr EFS of 22 pts with "CNS+" and M2-M3 marrow was 32± 10% compared with 40 ± 6% for 79 pts with M2-M3 without "CNS+" disease (p=N.S.). When 3-yr EFS for disseminated SNCCL pts was compared between CNS-/*M1 versus* CNS+/M1 *versus* CNS-/M2-3 *versus* CNS+/M2-3, the differences were significant (p=0.001). The relative risk for failure for patients with "CNS+" disease after adjusting for marrow status is 1.43 (95% CI= 0.9-2.3). We conclude that the presence of CNS disease at diagnosis does not clearly predict an unfavorable outcome independent of initial bone marrow status. CNS involvement as a component of initial relapse represents a significant problem, despite the use of CNS irradiation in the majority of pts.

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RISK FACTORS AND OUTCOME IN CHILDHOOD ALL CORRELATE TO DAY 29 RESIDUAL DISEASE MEASURED BY PCR OF CLONE-SPECIFIC IGH/TCR REARRANGEMENTS - NOPHO MRD-95 STUDY

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Leukemic lymphoblasts have rearranged immunoglobulin (Ig) and T-cell receptor (TCR) genes. These rearrangements are clonal and unique and thus applicable for the monitoring of residual disease (RD). PCR-analyses of the junctional regions of the IgH-, TCRγ-, and TCRδ-genes demonstrated one or more clonal rearrangements in 146 of 148 ALL patients (22 T-cell) included in the study. 58 patients with other malignant or non-malignant disorders were PCR-negative. The residual leukemia following 4 weeks of induction therapy (VCR/PRED/ADRIA/i.t.MTX) was determined by a new, competitive PCR-technique, which was clone-specific, sensitive (detection limit: 1:100.000), and precise (between-run variation: 2-fold or less at 1:10.000) PCR-technique. In patients with more than one clonal rearrangement, the measured RD was independent of which IgH/TCR-marker was applied. The median post-induction level of RD (RD_{day29}) for patients staying in remission was 0.007% (75% range: 0.001-0.3) vs 0.4% for patients, who experienced a relapse (p=0.002). The RD_{day29} was the strongest predictor of the risk of a subsequent relapse. The RD_{day29} was related to known prognostic factors in childhood ALL such as WBC (Spearman-r_S=0.47), age (r_S=0.36), and immunophenotype (T vs pre-B; median RD_{day29}: 0.6 vs 0.006; p=0.0001). Patients with a low day-7 blast count or a high DNA-index tended to have low RD_{day29}.

Conclusion: Since the clinical impact of well-known risk factors seem reflected in the day 29 residual leukemia when determined by the competitive PCR-technique this could be a key parameter for the stratification of post-induction treatment intensity. In addition, it could be applicable for rapid up-front identification of new risk factors and response to phase II drugs (and drug combinations), as well as for monitoring of RD following BMT.

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PRIMARY IMMUNODEFICIENCIES AND NHL IN CHILDHOOD - PATIENTS AND RESULTS FROM THE NHL-BFM-TRIALS

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Prospective analysis of children with primary immunodeficiencies diagnosed of NHL and treated according to protocols NHL-BFM 86-95 was performed aiming at a detailed description regarding clinical presentation, diagnostic features, therapy-strategies and outcome in this special patient population.

From 10/86 to 2/97, 18 of 1331 children with NHL enrolled in the NHL-BFM-studies suffered from primary immunodeficiencies (ID). Age at diagnosis of NHL was significantly lower than in NHL-patients without ID (median 6,5 vs. 9,1 ys.; p=0,04). A wide range of ID was observed with predominance of combined (N=12) over isolated humoral defects (N=6). Chromosomal instability-syndromes accounted for 7 of 12 combined defects (Nijmegen-breakage-syndrome (NBS) N=4; Ataxia teleangiectasia N=2; Fanconi anemia N=1). The remaining 5 patients with combined ID suffered from rare (PNP-deficiency N=1, IL2-rec.-defect N=1) or undefined combined deficiencies (N=3). Immunological studies revealed 12 lymphomas of B- and 6 of T-lineage. 6 of 12 pts. with combined ID were diagnosed of T-NHL, 6 of B-NHL. 2 of 6 patients with humoral defects presented with T- and 4 patients with B-NHL. All patients with NBS had B-cell-lymphomas. The distribution of NHL-entities was significantly different between ID- and non-ID patients (p=0,003): Centroblastic and immunoblastic lymphomas (27% vs 7%), anaplastic large cell lymphoma (27% vs. 5%), Burkitt-lymphomas (22% vs. 46% in non-ID pts.). 16 pts. received polychemotherapy, 7 with reduced and 9 with regular intensity. Therapy-toxicity was increased in ID- compared to non-ID patients. In 13 patients remission was achieved. 5 patients died during treatment (3 of tumor progression, 2 of sepsis), 2 patients relapsed and died; 1 patient died of BMT-related toxicity in first CR. 10 patients (4 with humoral and 6 with combined ID) are still in 1. CR after a median follow-up of 4 years.

Results from this analysis suggest that curative treatment of NHL in the presence of primary ID is possible and should be attempted. However, further cooperative studies are required to develop specific therapy strategies for patients with NHL and primary immunodeficiency.

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RISK-ORIENTED TREATMENT OF CHILDHOOD ALL: AN UPDATE OF MULTICENTER TRIAL ALL-BFM 90.

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2300 pts with childhood ALL (age ≤18y) from 97 centers in Austria, Switzerland and Germany were enrolled from 4/90 to 3/95 in trial ALL-BFM 90. Patients were stratified into three branches: standard risk (SRG), medium risk (MRG), and high risk (HRG). Stratification was derived from the concept of the previous trial ALL-BFM 86 (BLOOD 84, 3122 [1994]) based on initial leukemic cell mass and early response to prednisone. Treatment for SRG and MRG consisted of induction, consolidation with HD-MTX, and reinduction followed by maintenance therapy for a total treatment duration of 24 months. However, in contrast to trial ALL-BFM 86, anthracycline dose was reduced by 15%, IT MTX therapy was intensified, and prophylactic cranial irradiation with only 12 Gy was applied in MRG and HRG. In HRG, phase I of induction was followed by nine multidrug pulses utilizing HD-MTX, HD-ARA-C, antimetabolites, vinca-alkaloids, VP-16, ifosfamide, doxorubicin, and triple drug intrathecally. Two randomized questions were asked: I) MRG: Can pEFS be improved by high-dose L-ASP in consolidation? II) HRG: Can duration of neutropenia and number of febrile episodes be decreased by prophylactic use of G-CSF in HRG? 2195 patients are evaluable. 2149 patients (97.9%) achieved complete remission. 1.1% of patients died in 1st CR. 14.6% of patients suffered from relapse; recurrences with CNS involvement were observed in 2.7% of pts. After a median follow-up of 47 months, pEFS overall is 0.74 (SE=0.02). Patients treated in SRG (n=632) and MRG (n=1316) fared significantly better (pEFS 0.81 and 0.78, respectively) than patients in HRG (n=247, pEFS 0.34). HD-L-ASP did not improve the outcome for MRG, but in HRG the use of G-CSF reduced treatment morbidity. Early blast cell reduction as defined by prednisone response was the most suitable factor to separate high risk patients from any subgroup.

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PRECURSOR-B-CELL LYMPHOBLASTIC LYMPHOMA OF CHILDREN: TREATMENT AND RESULTS IN TRIALS NHL-BFM 86 AND 90

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Precursor-B-cell lymphoblastic lymphoma (PBLL) rarely occur as primarily extramedullary disorders. We analyzed frequency, characteristics and treatment results from 1075 patients (pts) with NHL registered in the two subsequent multicenter studies NHL-BFM 86 and 90 from October 1986 to March 1995. 29 pts (2.7 %), with a median age of 6.7 years (range 0.75-15) were diagnosed with PBLL. The male to female ratio was 2.2:1. Stages (St. Jude) were: I (n=3) and II (n=7), III (n=10) and IV (n=9; BM+, n=8; BM-/CNS+, n=1). 22 pts presented with peripheral LN, five pts with subcutaneous and one pt with periorbital (local only) manifestations. 23 pts were treated according to the BFM-ALL protocol: Pts with stage I and II received an 8-drug induction followed by extracompartment consolidation with methotrexate and maintenance therapy for a total duration of 24 months. Pts with Stage III and IV received additional reinduction and prophylactic cranial irradiation with 12 Gy (24 Gy for CNS disease). Five pts were treated according to the B-NHL protocol: Pts with stage I and II disease (resected) received three, while all others received six, 5-day therapy courses based upon dexamethasone, methotrexate, cyclophosphamide, ifosfamide, doxorubicin, cytarabin and etoposide plus intrathecal therapy. One pt with mucopolysaccharidosis died before treatment. All treated pts achieved remission. With a median follow-up time of 3.5 years, the estimated probability for event free survival (pEFS) for the total group is 0.68 (SE 0.11). Five pts suffered from relapses, 3/23 treated according to ALL-strategy and 2/5 treated according to B-NHL after a median time of 1.8 years (range 0.75 to 4.25) after diagnosis. Two pts had stage I, one had stage III and two had stage IV disease.
Precursor-B-cell lymphoblastic lymphoma account for approximately 3 % of NHL in childhood and adolescence. A characteristic feature are subcutaneous manifestations.Treatment based on ALL-strategy seems to be appropriate. Relapses occur even in localized disease.

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VINBLASTINE IS AN EFFICIENT SALVAGE TREATMENT FOR ANAPLASTIC LARGE CELL LYMPHOMA (ALCL).

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Objective : to study the outcome of children treated by Vinblastine for a refractory or relapsed ALCL.

Patients and methods : 11 patients aged 2 to 13 years (median 3.5 y) were treated with Vinblastine for a refractory or relapsed ALCL. Status of the patients at the beginning of Vinblastine was : primary resistant disease (1), first relapse (1), second relapse (5), third relapse (3) and fifth relapse (1). 6 patients had had a high dose chemotherapy with ABMT for consolidation therapy of a previous relapse.

Vinblastin was given weekly at a dose of 6 mg/m² for 6 months to 2 years (median 12 months). One patient received only 3 mg/m² twice a month. 4 patients also received corticosteroïds during 2 weeks to 2 months. This was the only treatment for all patients except one who received a course of high dose chemotherapy and ABMT as consolidation after 8 months of treatment with Vinblastine.

Results : Two patients had no evaluable tumor at the beginning of vinblastine, 8 patients achieved a complete (CR) and 1 patient did not respond and died 2 weeks after the beginning of the treatment. 5 patients relapsed : 3 of them at the end of the steroid therapy and 2, 18 m and 9 m after the end of the treatment (including the patient treated with ABMT as consolidation therapy). 5 patients are still in continuous CR with 11 to 30 months follow-up since the beginning of Vinblastin (median 20 months), 4 are of therapy.

Conclusion : Vinblastine is efficient in patients with ALCL highly treated and should be considered in front-line treatment and as maintenance therapy in high risk patients.

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CHILDHOOD HODGKIN'S DISEASE (HD): 25-YEAR EXPERIENCE AT THE ISTITUTO NAZIONALE TUMORI OF MILANO.

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Ob: to minimize sequelae from radiotherapy (RT) and alkylating agent-containing regimens, children with HD are now often treated with low-dose RT and potentially less toxic chemotherapy (CT). We performed a retrospective study comparing the results of three different protocols in which we reduced progressively fields and doses of RT, omitting Nitrogen Mustard. Methods: from 1971 to 1996, 194 consecutive patients < 18 years of age with newly diagnosed stage I-II-III HD were treated at Paediatric Division of INT of Milano. Study 1: before 1979 70 children (M 43 F 27; median age 10.7 yrs) staged by laparotomy with splenectomy, received extended field RT (35 to 45Gy) without (pathologic stage IA-IIA) or with CT (3 + 3 MOPP). Study 2: from 1979 to 1989, 85 children (M 59, F 26; median age 12 yrs), after clinical staging with liver and spleen biopsies in laparoscopy, were treated with CT (3 ABVD) followed by limited-field RT (30-35 Gy to involved nodal areas and 25 Gy to adjacent ones), plus 3 additional ABVD only to pts with B symptoms or stage III ± S. Study 3: from 1989 to 1996, 39 pts clinically staged (M 24, F 15; median age 13 yrs) were treated with CT (4-6 APVD, P = Prednisone instead of Bleomycin) followed by RT (25-30 Gy to involved nodal areas only). Results: for 70 children in study 1, OS, PFS and EFS at 10 yr (median follow-up, 21 yrs) were 83%, 76% and 61.5%, respectively. The corresponding figures for 10-year OS, PFS and EFS in 85 children of study 2 were 96.5%, 90.5% and 85%, respectively (median follow-up 13 yrs). For the 39 pts of the last study, 4 yrs OS and PFS were 100% and 90%, respectively. In the first study, 5 iatrogenic deaths occurred (sepsis 2, heart failure 2, second tumor 1); 9 pts developed second neoplasm and 7 pts developed major non fatal sequaele. In the second study, 2 pts developed second neoplasm (fatal 1) and 3 major non fatal sequaele. In the third study no severe sequaele have been reported so far, but follow-up is still too short. Res: we concluded that throughout the years OS and PFS improved and morbidity was decreased by omitting staging laparotomy with splenectomy, reducing radiation doses and fields and deleting alkylating agents.

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NON B-LYMPHOBLASTIC LYMPHOMA WITH BONE MARROW (BM) INFILTRATION: LONG-TERM RESULTS OF TWO CONSECUTIVE TREATMENT PROTOCOLS.

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Objective.Two treatment protocol results for non-B NHL with BM infiltration will be discussed. Methods and results. GROUP 1. From '79 to '89 15 pts (M/F ratio 2.75, median age 6.7 yrs) were treated using a 7-drugs 24 month-regimen (PDN, CTX, ADR, MTX, AraC, BLM, 6Tg) already adopted for stage III disease (Am J Ped Haematol Oncol '83; 5:161). Eleven children were affected by CD10/DR$^+$ NHL, 4 by T-cell NHL. All of the 15 pts presented > 25% BM infiltration, 9/15 peripheral blood invasion. Lymphnodes were involved in 11 pts, testis, kidneys and mediastinum in 2 each, Waldeyer ring in 1. No one presented CNS involvement at diagnosis. 3/15 received RT (dose: 25-30 Gy): CNS

prophylaxis (2), neck + Waldeyer ring (1), testis (1). 93% of pts obtained CR. 6/15 children (40%) were alive NED and EFS was 26% with a median f-up of 131 mos (range 97-196); median time to relapse was 25 mos. Of 11 relapses, 4 involved testis, 4 BM, 1 BM+liquor and 2 BM+liquor+mediastinum+nodes; 2/11 pts were salvaged and were NED at 136 and 160 mos from relapse. GROUP 2. Considering that 7/11 failures involved "sanctuaries", we intensified both induction and maintenance CT in a 18 month-program. HD-MTX 8 g/sqm 6-hour infusion was administered twice during induction phase and twice during reinduction at the end of the two 6-month maintenance phases, followed by Erwinia asparaginase 1000 U/Kg for 10 d, associated to AraC 200 mg/sqm every other day for 5 times. From 9/89 17 children (M/F ratio 4.66, median age 7.1 yrs) have been treated so far. Eight children were affected by CD10/DR+ NHL, 9 by T-cell NHL.14/17 presented >25% BM infiltration, 7/17 peripheral blood invasion. Lymphnodes were involved in 12 pts, bone and mediastinum in 7 each, Waldeyer ring in 5, cutis in 2; no one had CNS infiltration. One received RT to neck. 100% of pts obtained CR. 14/17 children (82%) were alive NED and EFS was 70% with a median f-up of 67 mos (range 3-89 mos); median time to relapse was 20 mos. Of 5 relapses (4 with T-cell subtype), 1 involved BM, 1 BM+lymphnodes, 1 BM+bone, 1 liquor, 1 mediastinum+lymphnodes; 2/5 pts were salvaged and were NED at 11 and 73 mos from relapse. Conclusions. Results of this intensive therapeutic program were satisfying as a whole, but for the T-cell subgroup (EFS 55%) we are planning a new treatment strategy.

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POSTTRANSPLANT LYMPHOMAS IN CHILDREN - REVIEW OF 3 PATIENTS TREATED WITH NHL-BFM-PROTOCOL

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Three children with post-transplant-NHL treated according to therapy-protocols NHL-BFM 90/95 are reviewed with respect to clinical features, viral studies, therapeutic management and outcome.

2 patients transplanted for congenital renal dysplasia more than six years prior to diagnosis of NHL received ciclosporin A (plus prednisone or azathioprine) and presented with primarily extranodal NHL. One pt. with Burkitt-like lymphoma showed disseminated disease with BM-infiltration; 80% of lymphoma-cells were positive for EBV-genome. The second pt. suffered from immunoblastic lymphoma and presented with gingival hyperplasia and infiltration of the paranasal sinuses. Both pts. received polychemotherapy according to protocol NHL-BFM 90/95 with dose-reduction of nephrotoxic drugs. Immunosuppression was omitted during chemotherapy. Both patients reached CR after 2 courses. Therapy-toxicity was limited, transplant-rejection did not occur. Both patients are in first CR 2 and 4 years after diagnosis. The third patient was a 2 ½ year-old girl presenting with centroblastic lymphoma of the adenoids, the paranasal sinuses and the jejunum four months after heart-lung-transplantation for pulmonary hypertension. Immunosuppression consisted of azathioprine, prednisone and FK506. The lymphoma was composed of mixed oligo- (adenoids) and monoclonal (jejunum) cellularity. EBV was detectable by PCR in BM-aspirates, but not in lymphoma-cells. Initial treatment consisted of change of the immunosuppressive regimen. Due to transplant rejection and tumor progression, polychemotherapy was started 4 weeks later. Modified NHL-BFM-therapy with dose reductions and omission of cardiotoxic drugs was administered. Remission was achieved after 2 courses. Therapy tolerance was limited with repeated sepsis and recurrent organ rejection. However, cardiac function was not affected.

NHL-BFM-therapy appears to be a safe and successful approach towards children with post-transplant NHL. Even children with advanced tumour stages seem to profit from intensive chemotherapy without jeopardizing the transplant. However, further experience is required to develop safe and efficient therapy-strategies for post-transplant NHL in children.

P-200

Minimal tailored treatment for children High Risk B cell N.H.L. (HRBCNHL) according risk factors for relapse - Brazilian Cooperative N.H.L. Group (BCNHLG).

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The objective of this study was to adapt the treatment intensity to different HRBCNHL risk groups.From march 94 to Jan 97, 67 previously untreated NHL children, from 10 institutions, were classified and treated according the following risk factors: a) **Low Risk for Relapse (LRR)** - LDH<1000, no bone marrow infiltration and or CNS involvement, no pleural effusion nor ascites and complete response after 1st chemot. cycle; b) **Intermediate Risk for Relapse (IRR)** - LDH >1000 and or +BM (<25%) and or nervous palsies, positive pleural and or ascites fluid or renal impairment; c) **High Risk for Relapse (HRR)** - L3 and or CNS involvement and all patients with incomplete response after 1st chemot. cycle. The LRR group received four cycles chemot. A-B-A-B. A (CTX+VCR+IDMTX$_{2g}$+PRED) B (VM26+ARAC) 3 to 4 months. The IRR received six cycles A-C-B-C-B-C. C (CTX+PRED+HDMTX$_{5-8g}$). The HRR group received five cycles A-C-D-C-E. D (IFO+ADR) - E(ARAC+HDARAC +VP16). The IRR pts and HRR received a cytoreduction with COP before cycle A 22 pts were classified as LRR, 31 IRR and 15 HRR. The overal survival was 70%. This first analysis show that this strategy was comparable to more intense treat. regimens. In addition cumulative doses of alkilators, anti-metabolites, anthracyclines and VP16 was smaller than those in the most used protocols (BFM and LMB). Treatment tailored for risk factors is an apropriate strategy for children HRBCNHL ensuring an optimal outcome and potentially decreasing long term toxicity mainly for LRR and IRR pts.

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DEXAMETHASONE, HIGH-DOSE CYTARABINE AND CARBOPLATIN (DAC) IS AN ACTIVE REGIMEN IN ADVANCED STAGE PEDIATRIC LARGE CELL NHL.

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Conventional treatment for large-cell non-Hodgkin lymphoma (NHL) relies largely on anthracycline and cyclophosphamide. To further improve treatment outcome by identifying effective treatment combinations, we have piloted a study which tests the efficacy of dexamethasone (40mg IV daily x 4), ara-C (2 gm/m^2 IV q 12h x 2 on day 2) and carboplatin (given intravenously and targeted to a systemic exposure of 8 mg/ml•hr on day 1) combination. This combination (DAC) was given for 2 courses, followed by multiagent consolidation and continuation treatment for a total duration of 10 months. From 1991 to 1996, 19 boys and 4 girls, 5 to 17 years of age with stage III (n = 20) or stage IV (n=3) large-cell NHL were treated with this combination. The DAC combination resulted in complete remission in 10 cases (43%) and partial response in 8 cases (35%). With additional treatment, 16 patients (70%) attained complete remission and 3 (13%) partial remission. To date, 14 patients remain in continuous complete remission for 6 to 63 months (median, 48 months). With retrieval therapy including autologous hematopoietic stem cell transplantation, 18 of 23 patients (78%) are currently alive and disease free. The DAC regimen was well tolerated. We conclude that DAC is an effective combination for large-cell NHL.

P-202

EFS, TOXICITY AND SUPPORTIVE CARE OF BFM90 PROTOCOLS FOR TREATMENT OF CHILDHOOD ALL IN GERMANY AND RUSSIA

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The introduction of the BFM protocol in the treatment of childhood ALL in Russia allowed to achieve promising results. But toxicity seemed to be more

severe than in western countries. Therfore, a comparison of toxicity related to ALL-BFM-90 protocol in Berlin and a modified protocol ALL-BFM-90M applied in Moscow was performed.

The modified ALL-BFM-90 utilized 1 g/m²/36h MTX instead of 5 g/m²/24h.

Between January 1991 and May 1995, 37 children in Berlin and 51 in Moscow have been treated in both, standard and medium risk group.

Kaplan Meier estimates for EFS at 5 years were not significantly different in Moscow and Berlin.

Duration of neutropenia, number of thrombocyte transfusions, alterations of liver enzymes and creatinine were similar in both groups. However, percentage of patients with haemoglobin < 70 g/l was significantly higher in BFM compared to BFMM. The number of erythrocyte transfusion was lower in BFM compared with BFMM. The use of i.v. antibiotic therapy along with antimycotic therapy was lower in BFM compared to BFMM together with need of inpatient treatment ($p<0.05$). Toxicity of protocol M was more pronounced in BFMM than in BFM.

Conclusion: BFMM was partly more toxic than BFM. Whereas a higher toxicity of 1 g MTX/m² at 36 h compared to 5g/m² at 24 h has already been described.

Russian children seem to suffer more from intensive chemotherapy than german children. One explanations might be a worse nutritional status as well as a different microbiological environment.

Supportive therapy seems to be applied earlier and more extensively in russian clinics.

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MEDIASTINAL LARGE B CELL TYPE LYMPHOMA (NHL). RESULTS OF THE FRENCH SOCIETY OF PEDIATRIC ONCOLOGY (SFOP) LMB89 PROTOCOL

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Since large B cell NHL primarily localized in the mediastinum is of rare occurrence in children, the SFOP NHL group decided in 1989 to treat them with the SFOP-LMB protocol, in an effort to standardize there treatment (Xt).
The Xt scheme (Arm B of LMB89, C.Patte et al, SIOP XXV Med Ped Oncol 21 : 531 ; 1993) consisted in a COP prephase, followed by 2 courses of COPAdM (MTX 3g/m2), 2 courses of CYM and 1 COPAdM. Patients with no response to COP were planned to receive the Arm C of LMB89 (2 COPAdM - MTX 8g/m2, 2 CYVE and 4 maintenance cycles). CR had to be verified in case of residual mass at the end of induction Xt. Histological subtype was reviewed as large cell. Nine patients (pts) (4M, 5F), age 6 to 16 (median 14) years at diagnosis were registered between 1989 and 1995. Eleven additional B-NHL of the mediastinum were also registered during the same period (5 Burkitt or Burkitt like, 6 High grade non classified), where 566 cases of B-NHL were treated by the LMB 89 protocol. The mediastinal mass was in all cases > 5 cm in the largest diameter. Other thoracic localization were : pleural effusion (4), pulmonary nodules (4), pericardium (3), chest wall (1). Outside the thorax, sites of the disease were: cervical LN (1), kidney (2), pancreas (1). Bone marrow and CSF were clear of malignant cells in all pts. In the evaluable pts, LDH serum level at diagnosis was lower or equal to twice the normal institutional upper value (3 and 4 pts respectively). All had Murphy Stage III. Response to COP was observed in 8/9; therefore, only one pt switched from arm B to arm C Xt. CR was achieved in 7 pts after consolidation, being documented in 6 of them by surgery of a residual mass. Failure was observed in 2 pts: 1 with an active mass after CYM1 achieved CR after a third line Xt and tandem high dose consolidation therapy (HDC) with ABMT, followed by Radiotherapy on the mediastinum, but died of Xt related pulmonary complications; the second in whom surgical exploration of a residual mass was non contributive progressed 2 months later and died of disease despite an initial response to salvage Xt followed by HDC and ABMT. No relapse was observed in the remaining 7 pts, with a median follow up of 35 months (24 to 43). Children with mediastinal large B cell NHL can be cured with the SFOP LMB protocols, without radiotherapy, as long as CR is achieved and histologically proven at the end of induction Xt.

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Outcome and toxicity of an ifosfamide-based soft tissue sarcoma treatment protocol in children. The importance of local therapy.

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Although the survival of children with soft tissue sarcoma (STS) has improved considerably over the last two decades, the outcome of children with metastatic disease, and those with primary tumours of the extremities or parameningeal sites remains disappointing. 22 children with STS (16 rhabdomyosarcoma) who presented with unresectable tumours were treated with five courses of ifosfamide (9 g/m^2) and etoposide (600 mg/m^2). Patients who did not achieve a complete response then received local therapy with either surgery or radiotherapy. Chemotherapy with ifosfamide combined with etoposide, vincristine (1.5 mg/m^2) and doxorubicin (60 mg/m^2) or vincristine and actinomycin D (1.5 mg/m^2) was continued for one year. Objective responses to five courses of ifosfamide and etoposide were seen in all patients. Disease free survival (DFS) at a median follow up of 55 months was 55% (95% CI 32-73%). The DFS at three years of children who received local therapy was 85% compared with 33% in those who received chemotherapy alone (p=0.01, Log Rank test). Locoregional recurrences did not occur in children who received radiotherapy to the site of the primary tumour. These results suggest that intensifying chemotherapy does not reduce the incidence of loco-regional recurrence in children who do not receive local therapy. The initial response rate to ifosfamide and etoposide was impressive and warrants comparison with other regimens.

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NON HODGKINS LYMPHOMA SURVIVAL IN PEDIATRIC AGE. EXPERIENCE OF GROUP GICOP.

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OBJECTIVES
The experience of the G.I.C.O.P. in pediatric survival non Hodgkin lymphoma diagnosed and treated by this group during fifteen years, is presented.

METHODS
The lymphoma diagnostic was based in the study of lynfocitary marking in ganglionar biopsy sample. Two therapeutic protocols based on immunophenotypic classification of non-Hodgkin lymphoma into type B or non B were used.
The treatment was basically the same during the study period; LSA2-L2 protocol was used for lymphoma non B and G.I.C.O.P. Burkitt-82 protocol for type B.
Statistical treatment: probability survival has been calculated by the Kaplan-Meier method and the comparations by the log-rank test.

RESULTS
Of 80 patients, 73 reached complete remision. Disease free survival for this 54 patients was 0,84 +- 0,04 SD to fifteen years, 68 patients remained free of disease.
In the group NHL type B the complete remision was 88,1% (37 of 42 patients). Disease free survival probability in this group is 0,88 +- 0,05 SD.
Making stadium difference, the disease survival probability to the groups I,II y III was 100%; to the patients of the group IV was 0,87 +- 0,06 SD.
The 37 patients of the group NHL type non B disease free survival probability was 0,81 +- 0,06 SD. By stadiums the disease free survival probability was 100% in the group I; in the group II was 0,80 +- 0,179 SD ;in the group III was 0,82+- 0,113 SD and 0,66 +- 0,157 SD in the group IV.

CONCLUSION
The results of our experience confirm important implications of immunological classification in order to apply an adequate treatment. The actual figures of disease survival probability were unthinkable ten years ago.

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Dispelling the Myths - Patient Information

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Primary Bone Tumours are rare in children, which makes it hard for patients to get up-to-date information covering their treatment. ROH is one of only two centres dealing with the staging and surgery of bone tumours in the UK.
For this reason, a need was identified for the families to have an information booklet to refer to while receiving the pre-surgery chemo., at their local oncology centre which is often hundreds of miles from Birmingham, as these centres are not familiar with the surgery.
To cover this deficit, a patient information booklet has been produced along an MDT approach as we are aware that, during the initial stage of an illness, denial may well interfere with the patient's learning as they are likely to suppress and distort information given to them. However, on returning home, they may begin to ask questions but, by this time, are many miles from the centre. Hope is based on knowledge not on ignorance and, as such, education helps the patient to become well-informed. The information given within the booklet discusses the advantages as well as the disadvantages of the different surgical options to, hopefully, allow the child and the family to make informed decisions about treatment.
The value of this booklet is being assessed by means of patient satisfaction questionnaires which are completed when the child returns for surgery and all comments made will influence the reprinting of further booklets.

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THE INCIDENCE OF ORAL COMPLICATIONS IN PEDIATRIC PATIENTS RECEIVING HIGH DOSE CHEMOTHERAPY

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In our institutional setting, oral hygiene of patients is often neglected, although we have been using very intensified chemotherapeutic protocols, recently. Extensive mucositis and ulcerations often develop in the mouth. During chemotherapy and / or radiotherapy, open ulcerations are a possible route for the entry of oral pathogens to the systemic circulation. Nearly 90% of our neutropenic patients show severe infections. The purpose of this study was to determine the incidence of oral complications in pediatric patients with cancer receiving chemotherapy and radiation therapy. Fifty children with cancer who were diagnosed between January 1st.1995 and December 31st. 1995 were followed for oral complications including oral ulcerations, fungal and viral stomatitis and mucosal bleeding. Other characteristics such as age, tumor type, therapeutic protocols were also noted. Mean follow-up is 8.0+/- 4.5 months. Oral complications were seen in 21 patients (42%). Commonest oral lesion was ulceration (48%). Fungal infection, bleeding and herpetic gingivo-stomatitis were seen 44%, 10%, 8% respectively. Patients with lymphoproliferative tumors showed a very high therapy- related oral complications. This frequencies were 100% in AML-BFM 90, NHL-BFM 90 and 86% in ALL-BFM 90 protocols. This ratio was 33% in combined ICE protocol which were used as a second - line protocol in resistant or relapsed solid tumors. Patients with solid tumors showed a less than 20% of oral complication rate with differrent combined chemotherapeutic protocols. This study shows that oral complications develop in a majority of patients and that nurses need to be aware of current scientific rationales that underpin good practice so that they can choose the most appropriate strategy of care to deliver.

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NURSING IMPLICATIONS IN THE TREATMENT OF NON-HODGKIN LYMPHOMA IN BRAZIL

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Objective: To highlight the nursing care of children with Non-Hodgkin Lymphoma (NHL).
Methods: We retrospectively reviewed the institution experience with NHL.
Results: We found 91 patients from November 1988 to December 1996. The age ranged from 2 years and 8 months to 18 years old. There were 60 boys and 31 girls. We had 4 patients with Burkitt's lymphoma and 87 patients with lymphoblastic lymphoma. They were admitted and treated with a multiagent chemotherapy and CNS protection was given in the induction phase and throughout treatment. Routine urine alkalinization was performed and careful nursing recording of liquid intake and output was done. The patients were observed closely during this time since infection is another primary threat. Following the maintenance therapy all patient care and monitoring was on an outpatient basis. This therapeutic schedule was successful as complication (lysis tumoral syndrome) and death rate was low.
Conclusions: Current aggressive therapy from the onset of treatment combined with appropriate nursing care in the inpatient and outpatient basis, have yielded high success rate to patients with NHL.

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STRESS EXPERIENCED BY MOTHERS OF YOUNG CHILDREN WITH NEUROBLASTOMA: CASE ANALYSIS BY USING JAPANESE VERSION OF PARENTING STRESS INDEX

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[PURPOSE] Children with neuroblastoma require the long-term hospitalization with their mothers for treatments. Nurses in the pediatric surgical unit have focused on stress reduction of mothers. The purpose of this study was to describe stress experienced by mothers of young children with

neuroblastoma. [SUBJECTS] Eight Mothers participated in this study and their ages were between 22 and 34 years old. Children with neuroblastoma were between ages of 10 and 36 months. The total lengths of hospital stay were between 3 1/2 and 36 months. Children with neuroblastoma had one or more of the following characteristics: requiring long-term hospitalization for treatment, experiences of bone marrow depression, requiring IVH. [METHOD] Abidin's (1986) Parenting Stress Index (PSI) was translated into Japanese and standardized by using 397 Japanese mothers of healthy children. The Japanese version of PSI was used to measure the stress level associated with care giving for children. Staff Nurses asked mothers to fill out PSI after informed consent. Medical and nursing records were used to interpret results of PSI. [RESULTS] Mothers experienced various degree of care-giving stress of children with neuroblastoma during the hospital stay. PSI was useful to analyze the characteristics of stress. Each case analysis will be presented by using PSI charts.

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THE PSYCHO - AFFECTIVE PROFILE OF THE CHILDREN WITH NON-HODGKIN'S LYMPHOMA

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Purpose: We have tried a classification of the psycho - affective modification at children with non-Hodgkin lymphoma.
Patients and Method: We studied thirty children with non-Hodgkin lymphoma aged between 5 - 13 year diagnosed at the Oncological Institute Cluj-Napoca (1993 - 1996). The socio - economical level was: good in 7 cases, medium in 13 cases and scarce in 10 cases. It has been evaluated: 1.the bio - psycho type by repeated psychological examination in individual condition (using the Luscher test, family test) and group conditions. 2.the behavior of the children based on aspect, communication, standing, affect, concerns (date from physicians, psychologist, nurse, family, community).
Results: Three groups have been identified: 1. At the beginning of the disease, 80% presented irritability, instability, anxiety, dysphoric reaction. 2. during the therapy 80% accepted situation due to a psychological preparation. 3. At the end of the therapy 80% identified themselves to the colletivity, 10% presented an isolation tendency and renunciation, 6% a negative attitude and 3,3% destructive and aggressive attitude.
Conclusions: We cannot speak about general reaction but only individual reaction, with a differentiation in ccordance to the gravity of the clinical picture, the treatment, the psychological profile and the ambiental constellation. Consultation and psychological directing (even psychiatric) are advised during the therapy.

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TREATMENT METHODS AND RESULTS OF COMBINED TREATMENT OF WIDE-SPREAD RETINOBLASTOMA

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Purpose of study. Usage of modern distant -therapy and quick electrons in combination with chemotherapy allows to follow the organospearing treatment in wide-spread stages of diseases, especially in bilateral affection.
Material and methods. In bilateral process in not-complicated cases the conservative therapy of both eyes was done the electronic booster was used with energy of 13 MEV, daily dose was 2 Gy, total dose was 50 Gy. At the same time it was a combination with CT: vincristin, cyclophosphamid, adriamycin for primary tumor, metotrexat and cisplatin - for relapse, i.v. in standart doses, 6-8 cycles during 24 months. Attempt of conservative therapy without enucleation was undertaken in 166(70%) of 236 children including bilateral process - 89 pts. Stage T3 of the disease was diagnosed in 85% in one or both eyes.
Results. Full or partial regression tumors without signs of disease during 2 and more years was reached in 65% of events. Rest of the tumor continued to grow average every 12-18 months from the beginning of treatment and the enucleation was made. There were no relapses in bilateral affection. Five year survival with unilateral retinoblastoma pts with or without enucleation formed 92% and 82%. In bilateral cases there were 83% and 84% respectively.
Conclusion. Conservative therapy on the first stage of treatment does not influence upon the length of children's lives, but at the same time allows to save an organ of vision in more then half of pts even in T3 stage, which is very important in bilateral process.

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RENAL CELL CARCINOMA - REPORT OF 12 CASES

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Although Renal Cell Carcinoma (RCC) is the most common primary malignancy of the kidney in adults, it occurs rarely in children. We report 12 cases of RCC diagnosed at the Johannesburg & Baragwanath Hospitals, Johannesburg between 1988 & 1996. The tumor occurred exclusively in the African patient. The mean age at diagnosis was 10,1 yrs (range 5,6-12 yrs) & the male to female ratio was 0,7:1. Clinically no patient had hypertension & only 2 presented with an asymptomatic abdominal mass. The tumor presented with abdominal pain in 4, an acute abdomen after trauma in 1 and gross haematuria in 5. However, 66% patients had evidence of haematuria on urine examination & 5 had a haemoglobin of less than 9g/dl. 1 case was associated with tuberous sclerosis. Radiological appearance of the tumors did not distinguish the tumors from Wilms tumor. Staging was done according to NWTS staging for Wilms tumor. There were 4 Stage II (one bilateral disease), 6 Stage III (3 microscopic nodal, 1 gross nodal, 1 capsule penetration & 1 rupture) and 2 Stage IV (both liver). Overall 60% survive disease-free. 3 were biopsied only & all have died of their tumor. 2 patients (including the bilateral RCC) were treated with primary surgery only: both survive. 7 patients were treated with primary surgery, radiation and/or chemotherapy. Chemotherapy used was NWTS 3-DD protocol. The radiation dose varied from 10,8Gy to 46Gy. 5 of these patients survive. It appears that radiation in a dose of more than 36Gy may benefit microscopic residual and nodal disease. 2 patients were treated with preoperative chemotherapy with no response, & therefore the role of chemotherapy in RCC is in doubt. One case was treated with alpha-interferon on relapse which appeared to slow but not prevent disease progression. This form of therapy needs to be explored in the future.

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The influence of CD34 - antigen expression on children ALL treatment results: modified BFM-90.

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The aim of this study was to estimate the clinical significance of stem-cell ALL immunodiagnosis in childhood.
Patients and Methods: There has been studied 159 children with ALL. Expression of CD34-antigen took place in 32,1% cases. The results of treatment were estimated. We compared 2 groups of patients:
1. 24 patients treated by the BFM-90 programme (in modification)-protocols: I, M (MTX-1 g/m sq), II.
2. 18 patients treated by the BFM-90 programme (in modification)-protocols: I, M (MTX-1 g/m sq).
Results: In a group of stem cell leukemia (SCL) significantly higher levels of CD38, CD10, CD13, CD33 and CD22 were noted. The frequency of ' genuine' CL (which hasn't lineage markers) was low (2,3%).In the second group, expression of CD34-antigen didn't influence relapse-free(p=0,4) and overall (p=0,4) survival. In the first group significantly lower relaps-free survival (p=0,06) as well as overall survival (p=0,02) was noted in CD34+ cases. In CD34 +ve group 61,8% of patients were alive in 4-year follow up period, while in CD34 -ve group 84,5% of patients were alive.
Conclusion: This preliminary date show the significance of CD34 - antigen estimation in childhood ALL treated with intensive protocols.

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GUIDED FINE -NEEDLE ASPIRATION BIOPSY VERSUS SURGICAL BIOPSY OF ABDOMINAL SOLID LESIONS SUSPECTED OF MALIGNANCY

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This study evaluates the efficacy of guided fine -needle aspiration biopsy for the diagnosis of abdominal malignancies, in comparison with the opened surgical biopsy. Twenty five children with abdominal masses suspected to be malignancy by computerized tomography evaluation, were subjected to guided fine needle aspiration biopsy as well as surgical exisional biopsy.The biopsies were subjected to cytological and histopathological evaluation.Our results showed that,with guided fine needle biopsy,the cytological diagnosis was conclusive in 17 cases [68%] (11 children with malignant lymphoma ., one child with bilharzioma ., other child with rahbdomyosarcoma., 2 cases with neuroblastoma and two cases with non specific inflammatory lesions).While,5 cases (20%) suspected to have malignancy by guided fine needle aspiration biopsy without identification of the nature of malignant cells. While, false negative results were recorded in 3 cases (12%) with guided fine needle aspiration biopsy..In conclusion Fine needle biopsy of abdominal masses should be consisered in the diagnosis of the abdominal masses, since it is assosciated with higher success rate of true diagnosis of abdominal malignancy with lower rate of false negative results.

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LARGE CELL ANAPLASTIC LYMPHOMA IN CHILDREN

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Large cell anaplastic lymphoma (LCAL) or Ki-1(+) has been diagnosed since 1992 in our hospital. LCAL is defined by the presence of characteristic histologic features and CD 30 (Ki-1) expression.

Material and Methods. 6 pts (4 boys and 2 girls) with LCAL were treated between January 1992 and February 1995.Median age was 12.5 years (7-16). In three cases of six LCAL was previously misdiagnosed (Hodgkin's disease, T-cell NHL, and cat scratch disease). LCAL was proved by reviewing slides and immunophenotyping. By stages (Murphy) 1 pt had I stage, 1 pt — II, 1 pt — III and 3 pts — IV. In cases of stage IV, 2 pts had large skin involvement, 1 pt — multiple bone lesions. We did not observe any bone marrow or CNS disease. All pts had lymphadenopathy and 5 of them in addition fever (38-39 °C) for more than 10 days. Treatment was carried out according to modified BFM-90 (for B-cell NHL) protocol. One pt died of treatment related complications. Three pts had poor response to treatment and in spite of intensification of chemotherapy tumor progression occurred. Only two pts (including 1 pt with multiple bone lesions) had complete response and are alive disease-free with follow-up of 14-51 months.

Conclusion. Our results based on a few cases indicate that LCAL is a highly malignant tumor with variable clinical presentation. Lymphadenopathy and fever are most common. Complete remission may be achieved by using treatment protocols for B-cell NHL.

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STAGING LAPAROTOMY FOR PAEDIATRIC HODGKIN'S DISEASE : A RETROSPECTIVE STUDY OF 18 CASES FROM INDIA.

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Between 1978 to 1984, 18 children (M=12;F=6) with biopsy proven Hodgkin's Disease (HD) underwent a staging laparotomy (SL) to study the correlation between clinical stage (CS) and pathological stage (PS). Their median age was 11 years (range:6-15). Blood & biochemical studies, chest X-ray, bone marrow aspiration and biopsy were undertaken in all and lymphangiography in 6 patients while few had abdominal CT Scans & USG. Lymphocyte Predominance (LP) and Mixed Cellularity (MC) were seen in 7 patients each, Nodular Sclerosis (NS) in 3 and 1 remained unclassified (UC). Supradiaphragmatic HD was seen in 15 cases (CS IA-6;IB-3;IIA-4;IIB-1;IIIA-1) and barring 6 in CS I & IIA (LP-4;MC-1;UC-1) SL caused upstaging of all 4 in CS I & IIB to PS IIIB (LP-2; NS-1; MC-1). Of the 3 infradiaphragmatic HD cases, 1 each in CS IA (MC) & IIA (NS) changed to PS IIA and IV A respectively while 1 remained in IIB (LP). The 6 PS I & IIA cases were treated with Mantle RT (35-40Gy) and 4 remained controlled for a median of 36 mths., 1 died and 2 were lost to follow-up after completing therapy. All other cases were treated with standard COPP or ABVD regimens and involved field (IF) or total nodal irradiation and 9 remained disease free for a median of 35 mths., while 2 died during chemotherapy (CT). The median follow-up for the entire series was 35 mths. There were no acute complications of SL and late therapy effects included

growth defects and hypothyroidism with RT and hypogonadism with CT. Based on these results, our current policy for childhood HD is to treat with multidrug CT and IFRT without the use of SL or extended RT portals.

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THE RESULTS OF TREATMENT OF NEPHROBLASTOMA IN CHILDREN DEPENDING ON THE LOCAL PREVALENCE OF THE TUMOR

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The aim of the research was the retrospective analysis of the results of treatment of nephroblastoma and discovery of the most significant prognostic factors depending on radicality of the surgical excision and the local prevalence of the tumorous process.

Patients and Methods: 289 children, that have received complex treatment in connection with primary unilateral neproblastoma are included in the research. In overwhelming majority of patients - 254 (87,9 %) a tumor didn't extend outside its own capsule. But even in an integrated capsule interlocking of a tumor with surrounding organs was often observed - 144 (56,7 %) cases. The most frequently the adrenal gland, perirenal fat, the diaphragm, the mesentery and the spleen were involved in the process - 19,5 %, 15,0 %, 12,7 %, 12.0 % and 3,4 % respectively. Out of 254 patients with an integrated capsule in 21(8,3 %) cases there was rupture of the capsule. Tumorous invasion of the hilus was observed in 9, the tumor thrombus in the renal vein-in 1, in the inferior vena cava - in 4, penetration of a tumor into the ureter - in 5 cases.

Results: Study of remote results of treatment is carried out according to data of 270 children with verified catamnesis. The 2-year relapse-free survival (RFS) made 65,6 % (169 patients). In case of extension of a tumor outside its own capsule the 2-year RFS was reduced nearly twice. In case of infiltration of the hilus the 2-year RFS made 37,5 %. Rupture of a tumor capsule brought to relapse in 14 cases out of 21. Exploratory puncture of a tumor didn't worsen the 2-year RFS while excisional biopsy reduced it to 28,6 %. In case of affected regional lymph nodes the 2-year RFS made 35,7 %.

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CHILDHOOD NHL IN IRAN

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NHL ranked as the 3d common malignancy after ALL and RB in children, who frequented our hematology/oncology dpts in the past 15 yrs. In a retrospective study, medical records of 374 pts were reviewed. There were 271 males and 103 females (M:F ratio 2.6 %) with an age range of 1.5 to 16 yrs (mean age 7 yrs) . All pts underwent standard laboratory & imaging work - up and clinical and by indication surgic-al staging procedures . Histolog . classification was made according to Rappaport and later to the working formulation . Immunophenotyping was carried out whenever available . The main clinical features were : primary abdominal tumors in 2/3 of pts , cervical and mediastinal tumors came next , primary tonsilar affection occurring in 3 pts. One hundred and thirty five pts (36.1 %) had B cell (Burkitt's type); 62 pts (16.6 %) lymphoblasic T cell ; 20 pts (5.3 %) well differentiated lymphocytic and 157 (41 %) large cell and undifferentiated NHL. The majority of pts with B cell lymphoma and most of other pts had stage IV disease at diagnosis.The management comprised chemotherapy and radiotherapy in case of B cell and bulky tumors unresponsive to the chemotherapy . This comprised LSA2L2 for T cell , LMB for B cell and COMP for lymphocytic lymphomas.Pts with B cell lymphoma had the highest mortality rate (23.7 %).
CONCLUSION : 1) Low socio-economic & nutritional status and delayed referal to pediatric cancer centers may have contributed to the high stage of NHL,2) High incidence of Burkitt's type NHL but no regional clustering of any especific type , 3) Stratification according to the histology and immunophenotypes and respective chemotherapy have improved overall survival and life expectancy in NHL.

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UP-DATED EPIDEMIOLOGY OF BURKITT'S LYMPHOMA (BL) IN CÔTE D'IVOIRE BASED ON 83 NEW CASES

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Objectives: The purpose of this study was to determine whether there has been a change in the previously reported prevalence of BL in wooded areas vs. the plains (savannah).

Patients and Methods: Between January 1994 and December 1996, 83 children: 46 males and 37 females, aged from 3.5 to 15 years with a median age of 7 years, were diagnosed as having BL on the basis of cytological and histological criteria, and clinical work-up. This consisted of routine blood studies, lumbar puncture, bone marrow smear, chest-x-ray films, ultrasonography and CT scans. The residence of the patient's family when the disease occurred was then plotted on a map.

Results: Seventy-six patients (91%) came from wooded areas and 7 from the savannah, corresponding to an incidence respectively of $5.4/10^5$ and $1.6/10^5$ inhabitants. Previous reports* had estimated the incidents to be $5/10^5$ and less $1/10^5$ inhabitants for the wooded and savannah regions respectively.

Conclusions: The high prevalence of BL in wooded areas vs. the savannah remains stable.

Significance: This observation encourages the initiation of an efficient, cost-effective national program focused on the wooded areas of the Côte d'Ivoire designed (1) to control possible insect vectors, and (2) to improve surveillance measures and thus enhances early diagnosis and treatment.

*Rain et al.: J Exp Clin Cancer Res 2:213, 1983.

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FLOW CYTOMETRIC (FCM) IMMUNOPHENOTYPING AND DNA ANALYSIS IN ACUTE CHILDHOOD LEUKEMIA IN EGYPT .

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This work aimed to determine immunophenotypic expression of leukemic cell surface antigens , DNA ploidy and degree of cell proliferation in childhood acute leukemia using flow cytometry and to correlate these parameters with the response to therapy and prognostic factors .
Sixty infants and children , 31 males and 29 females , 6 months to 18 years old with a median of of 7.6 years were studied .
The diagnosis and initial classification were based on clinical history , clinical examination and cyto-morphological criteria(FAB) . Immunophenotyping and DNA ploidy status and measurement of cell% in S phase fraction were determined by FCM. ALL was diagnosed in 80.5% and AML in 19.5% of patients.
B lineage was diagnosed in 80.5% . CD19 was the most frequently expressed marker (87.9%) followed by CD10 (72.7%) . T ALL was found in 19.5% with CD2 and CD7 expressed in 87.2% , followed by CD5 in 75% . In myeloid lineage CD13 was expressed in 94.7% followed by CD33 in 73.7% . Mixed phenotypeis were found in 53.3% of patients . DNA Aneuploidy was detected in 33.3% , median % of S phase was similar in ALL and AML .
Patients with SPF >= 5% had a poorer survival rate than those with < 5% . The hyperdiploid lines in ALL showed the best prognostic criteria . In conclusion , immunophenotyping and DNA analysis help in defining the type , response to therapy and prognosis of patients with acute leukemia.

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SECOND MALIGNANCIES AMONG BULGARIAN CHILDREN

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The present study was undertaken to evaluate the frequency of second malignancies (SMN) in Bulgaria following treatment for cancer during childhood. Among 2 million children's population, in Bulgaria the newly diagnosed cases with cancer are 250 annually. During the period 1986-96 20 children with SMN have been diagnosed in our Clinic. Nine of them were girls, 11 - boys (1:1.2) The SMN appeared in a period of 1.5 to 17 years after the treatment for the primary neoplasm. Following are the first and second malignancies by patients: ALL - NHL (3 pts.); ALL - CML (1); ALL - Astrocytoma (2); M.Hodgkin - Astrocytoma (1); M.Hodgkin - ANLL (1); NHL - ALL (2); Neuroblastoma - RhabdomyoSa (2); Neurobl. - ALL (1); Bil. Retinoblastoma - RhabdomyoSa (1); Ewing's Sa - ANLL and ALL (2); Wilms Tu - RhabdomyoSa (1); Optic glioma - Ovarian Ca (1); Seminoma - NeurofibroSa (1); Neurobl. - Ganglioneurobl (1).
Familial cancer was registered in 5 cases among parents and children and in 3 cases among sibs; in 5 cases Recklinghausen's fibromatosis was diagnosed; in two of the cases the patients had identical twins. Nineteen cases had radiotherapy in the past and in 8 of them the SMN developed in irradiated area. Seventeen children were treated with alkylating agents, 2 received VP-16 and in 2 a splenectomy was performed.
Four children with SMN are still alive and 2 are long survivors (>5 and >10yrs.) The trail indicates that in Bulgaria every year 2 SMN are registered in patients treated during childhood for cancer. The risk factors for development of SMN, such as genetic, radiation and certain chemotherapeutic agents are discussed.

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A REVIEW OF 147 ORBITAL SPACE OCCUPYING LESIONS IN CHILDREN

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Orbital space occupying lesions in children range from benign cystic lesions to malignant neoplasms. Toward determining the distribution of the various pathologic processes and the trends over time, 147 orbital space occupying lesions in pediatric patients encountered during a 30 year period were reviewed. In this series, the five most common space occupying orbital lesions were secondary and metastatic tumors (32 cases, 21.8 %), rhabdomyosarcoma (24 cases, 16.3 %), vascular lesions (21 cases, 14.3 %), inflammatory lesions (21 cases, 14.3 %) and cystic lesions (19 cases, 12.9 %). The distribution of lesions in the first half (1966 - 1980) and in the second half (1981 - 1996) of the experience were compared. The most common lesion in the first half is secondary and metastatic tumors wherease vascular, inflamatory and rhabdomyosarcoma were the most common lesions in the second half. The percentage of secondary and metastatic tumors fell from 50 % in the first half to 14 % inthe second half. This difference seems to result from earlier recognition and treatment of primary neoplasms, especially retinoblastoma.

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COMPARISON OF SERUM MTX CONCENTRATIONS BETWEEN 1 G/M^2 VS. 3 G/M^2 MTX THERAPY IN ALL AND NHL PATIENTS.

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Monitoring of serum MTX concentrations (MTXc) is mandatory in high-doses because MTXc and clearance are correlated with prognosis.However many centers in developing countries may require HDMTX dose modifications due to drug toxicity.The aim of this prospective study is to determine whether 1 g or 3 g/m2 of MTX provides effective serum MTXc.
Patients and Methods:Previously untreated ALL (n:26) and NHL (n:7) cases diagnosed from September 1995 to December 1996 were enrolled. All pts. received BFM-90 ALL / NHL therapy with MTX dose modifications.The dosage was 1 g/m^2 in ALL (n:80 courses) and 3 g/m^2 in NHL (n:24 courses) given by 24h infusion.Serum MTXc were measured up to 96 h by homogenous enzyme immunoassay (Emit-MTX,Syva).
Results:Steady-state serum concentrations (Css) were 58±40 (median 40μM) and 17±16 (median 11μM) in NHL and ALL pts. respectively (p<0.01). In ALL group 66% Css were less than 10μM. Mean MTXc at 48h was significantly higher with higher dose of MTX (10±8 vs.0.7±0.5μmol/L,p<0.01).There was no difference between two groups at 72h. Systemic clearance of MTX was found higher in ALL pts (142±90 vs. 105±75 ml/min/m^2,p<0.05). No severe toxicity was observed either group.
Conclusion:These preliminary results suggest that 1g/m^2 of MTX seems not optimal to achieve effective serum MTXc reported previously. Relatively fast drug clearance also may increase the relapse risk. Although we can not give survival rates due to short follow-up time,we believe that 1g/m^2 of MTX dosage may influence long-term prognosis negatively.

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DRUG RELATED TOXICITY WITH MODIFIED BFM-90 PROTOCOL IN ALL AND NHL PATIENTS

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The usefullness of cancer chemotherapy is often limited by toxic reactions.Dose modifications may be required in developing countries

due to poor supportive care. This may worsen prognosis although life-threatening complications are lowered. Our current protocol for ALL and NHL is BFM-90 with modified MTX doses from 5g/m^2 to 1g/m^2 in ALL vs 3g/m^2 in NHL. The aim of this study is to evaluate the toxic effects of this protocol and whether MTX dosage could be safely increased to 5g/m^2.
Patients and Methods: 41 pts. with ALL and 12 with NHL from 1993 to 1996 were enrolled. Total of 330 courses (ALL:262 and NHL: 68) were evaluated according to WHO-recommendation for grading toxicity.
Results: The total toxicity of all courses is shown in the table.

Toxicity (%)	Grade I+II	Grade III+IV	Total
Myelosuppression	4	6	10
Anemia	-	10	10
Neutropenia	22	11	33
Thrombocytopenia	4	4	8
High AST-ALT levels	15	4	19
Neurotoxicity	-	2	2
Mucosal	3	2	5
Nausea-Vomiting	6	4	10
Allergic	2	6	8
Infection	7	8	15

The most common problems were elevation of transaminases and infection. High AST-ALT levels could be related to high incidence of hepatitis B and C which was 23% in our pts.There were no renal, pulmonary and cardiac complications observed. 3 ALL pts. died of infection. The data did not differ between two groups (p>0.05).
Conclusion: Both infection and hepatitis B and C are major problems. However our results suggest that 3g/m^2 of MTX dosage is well tolerated as 1 g/m^2. Therefore, we conclude that 5g/m^2 of MTX infusion could be safely applied to achieve better prognosis in the long-term period.

Objectives : To review the histologic characteristics and treatment outcome of children with non-Hodgkin's lymphoma (NHL) in Hong Kong.
Methods : Retrospective chart review of paediatric patients (<15-year-old) who was diagnosed to have NHL in two of the five major public hospitals with paediatric oncology service in Hong Kong. The study period span from Jan. 86 to Dec. 96. The histologic classification was based on Working Formulation guidelines and the clinical staging was according to the St. Jude system. Children who were diagnosed to have NHL after 1992 received UKCCSG-NHL-91 protocol and those who were diagnosed before 1992 received either LSA2-L2 or LMB-86 protocols.
Results : In this 11 years period, 29 patients were diagnosed to have NHL but only 27 patients
received treatment in our units. Of these 27 patients, all were ethnic Chinese and 17 of them were male. Their median age was 8-year-old (range 2.5 to 14 yr). 10/27(37%) had lymphoblastic NHL (Stage I : 2, II : 1, III : 1, IV : 6); 6/27(22%) had small non-cleaved NHL, all Burkitt's type (Stage II : 4, III : 2) and 11/27(41%) had large cell NHL(Stage I : 2, III : 7, IV : 2). 5/11 large cell NHL were Ki-1 positive NHL and 6/11 were large non-cleaved cell NHL. Two of our large non-cleaved cell NHL patients had underlying primary immunodeficiency. For treatment, 20/27 were treated with the UKCCSG-NHL-90 protocol; 3/27 were treated with LSA2L2 regimen and the other three received LMB-86 protocol. According to the UKCCSG-NHL-90 protocol, patients with lymphoblastic NHL were treated with the protocol designed for T- acute lymphoblastic leukaemia. One patient with stage I NHL was treated with surgery alone. Our overall event free survival was 78% with a median follow-up period of 3 year (range 1 to 10 year). According to the histologic classification, the event free survival of the advanced disease (Stage III & IV) were 43% for lymphoblastic NHL (median follow-up : 5 yr), 100% for small non-cleaved cell NHL (median follow-up : 7.5 yr) and 78% for large cell NHL (median follow-up: 3 yr). All of our early stage NHL patients survived. Of the 6 patients who relapsed (4 lymphoblastic, 2 large cell), 2 were salvageable with chemotherapy again. Two of our long term survivors had therapy-related cardiac complications and one of them required regular anti-failure treatment.
Conclusions : The distribution of the histologic subtypes of our paediatric NHL patients are similar to the other countries. NHL in children is a highly treatable disease and with current chemotherapy regimen, around 80% of the patients can be cured. We reviewed our local experience and with the exception of advanced stage lymphoblastic NHL, our treatment result was comparable with the published results.

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IMPAIRED RESPONSE TO rh HEPATITIS B VACCINE IN CHILDREN RECEIVING ANTICANCER CHEMOTHERAPY

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PURPOSE: The aim of this study is to evaluate the efficiacy of rh Hepatitis B vaccination for the prevention of Hepatitis B infection in different malignancies and chemotherapy regimens.
PATIENTS AND METHODS: Serologic responses to rh Hepatitis B vaccine were investigated in 50 pediatric cancer patients ages between 2 and 15 years. 20 of the patients were with hematologic malignancies, 30 with various solid tumors. 34 patients were receiving intensive and 16 mild or modarete chemotherapy. Vaccination begun within one month following the diagnosis. Three doses of rh Hepatitis B vaccine (40 mcg) were given at 0, 1, 2 months and a booster dose was planned at the first year. Periodic serologic follow up by quantitative antibody titers were performed one month after each vaccination and also in the 5th and 12 th month after vaccination. A titer equal to or greater than 10 mIU/ml were considered seropositive.
RESULTS: The seroconversion rates after the first, second and third doses were 0%, 13%, 21% respectively. Among solid tumors only two patients with Wilms tumor, one patient with brain tumor and among hematologic malignancies only one patient with acute lymphoblastic leukemia produced positive seroconversion. The patients who were receiving intensive chemotherapy gave weaker responses than the patients who were receiving mild or moderate chemotherapy.
CONCLUSION: The response is better in patients with solid tumors than in patients with hematologic malignancies. In addition the response is better in patients receiving mild or moderate chemotherapy. As a whole response is not effective, therefore combined administration of rh Hepatitis B vaccine and Hepatitis B immunoglobulin is needed.

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Paediatric Non-Hodgkin's Lymphoma : The Experience of two Hong Kong Cancer Centres

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COMPLICATIONS OF EXTERNAL RIGHT ATRIAL VENOUS CATHETERS IN PEDIATRIC CANCER PATIENTS

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The administration of chemotherapy and frequent blood sampling during the treatment of cancer patients have been greatly simplified and facilitated by the use of right atrial catheters (RAC). However, there are complications to indwelling catheters, including obstruction, dislodgement, and catheter-related infection. Furthermore, due to the differences in the rates of complications of the practice of oncology in developing and western countries the complications of the use of RAC needs to be determined and discussed in this perspective. The purpose of this study was to assess the frequency of mechanical and infectious complications of external RAC in pediatric cancer patients at Ankara University School of Medicine, Turkey, and to compare our results with those reported from developed countries. The records of all the pediatric oncology patients with external RAC was reviewed to obtain data on primary diagnosis, duration of catheter, mechanical complications of catheter, and the frequency of catheter infections. From 1993 to date, a total of 51 catheters were placed in 37 patients. Individual catheters were in place for a median of 173 days, with a total experience of 8822 catheter days. Only 32% of the catheters were removed electively. The overall rate of "clinically significant" infection was 12.2 per 1000 catheter days, with Staphylococcal species predominating. Approximately 19.6% of the catheters were affected by a complete "traveling cuff." Three catheters were complicated by leakage in the external portion and 3 in the internal portion. Partial occlusion affected 25.5% catheters, but complete occlusion was only seen in 3 catheters. In conclusion, in this study mechanical and infectious complications of external RAC were seen more frequently than reported for developed countries. These results will be discussed in perspective to oncology practice in a developing country.

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CHILDHOOD HODGKIN´S DISEASE IN ARGENTINA: a single institution experience.

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The purpose of this retrospective study is to give an overview of childhood Hodgkin's disease and the incidence of EBV in our population . From 1982 - 1995, 41 clinically staged children have been treated and followed- up at a single institution. Staging was carried out by a variable combination of chest X ray, CT scan, abdominal ultrasound, lymphangiogram and more recently gallium scan without staging laparotomy and splenectomy.

There were 27 boys and 14 girls (1.9 :1). Median age: 11 years (range 3-18 yrs); 9 pts were under 6 years. The histologic patterns were : mixed cellularity 18 pts (44%), nodular sclerosis 12pts (30 %), lymphocytic predominance 10 pts (24 %), and lymphocytic depletion 1pt (2%). Clinical stage: 7 pts IA, 13 IIA, 1 IIB , 9 IIIA, 1 IIIB, and 10 IV B. Thirty-three pts were evaluated for EBV presence by RNA/ RNA in situ hybridization for EBV oligonucleotides (EBERs), thirty-one pts were EBV positive (94%). Only two pts were negative (IA MC, and IIA NS). No difference was found among the different histologic subtypes. Chemotherapy (COPP- ABVD) was used in all the pts, combined with radiotherapy in 16 pts . Forty pts achieved complete remission (97.5%), 5 children subsequently relapsed, 4 of whom remain well, in second remission after alternative treatment, one patient refused further therapy. Median time of relapse was 1 year (1-14 years). The overall survival was 95% with a median follow up of 5.5 years (1-15 years).There has been no secondary leukemias or solid tumors.

The clinical outcome was excellent even in patients with advanced disease. The EBV is present in high proportion in childhood Hodgkin´s disease in our area; it does not seem to have prognostic implications.

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INTRATHECAL CHEMOTHERAPY IN CHILDHOOD RETINOBLASTOMA: AN 8-YEAR EAMC EXPERIENCE 1989 - 1996

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In an 8-year period, 32 patients were diagnosed to have Retinoblastoma. Patients with intraocular tumors were staged according to the Reese Ellsworth staging and those with extraocular tumors by the St. Jude staging. All patients were treated with VAC regimen (Vincristine, Doxorubicin, Cyclophosphamide) for a year. Group A (14 patients) diagnosed from 1989 to 1992 were not routinely given prophylactic intrathecal chemotherapy consisting of monthly Methotrexate as compared to Group B (18 patients) seen from 1993 to 1996 who were. All patients with positive CSF cytology, 11 (Group A) and 5 (Group B) were treated with triple (Methotrexate, Cytosine Arabinoside and Hydrocortisone) until negative. Results showed that occurence of CNS metastasis is higher in Group A 11/14 (75%) vs Group B 5/18 (30%). The response to triple IT is better in Group B, 4/5 (80%) as compared to Group A 5/11 (45%). The overall survival is 57% (8/14) in Group A and 83% (15/18) in Group B with a mean follow-up of 33.6 months and 42 months in Group A and B respectively. We conclude that prophylactic intrathecal chemotherapy using Methotrexate alone is effective in preventing CNS metastasis among these cases. Triple IT (Methotrexate, ARA-C and Hydrocortisone) is likewise effective in controlling CNS metastasis. Early diagnosis is still the best prognostic factor to ensure the success of treatment in Retinoblastoma.

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THE PRESENT SITUATION OF PEDIATRIC ONCOLOGY IN AFRICA

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Oncologic diseases are difficult to treat in developing countries, requiring vast resources and high degree of organization. In many parts of Africa the status of these diseases is still unknown.

A questionnaire is made and distributed to more than 100 centers and doctors interested in Pediatric Oncology in the continent aiming to understand magnitude of the problem, to know the relative frequency and pattern of tumors occurring in childhood and what is available and what is not available in different areas of Africa.

Lymphomas and Leukemias constitutes the main bulk of pediatric oncology problems, Retinoblastoma are typically more common in the southern parts of the African continent . Brain tumors appears to be underestimated in most countries.

In many of the sub-Saharan, areas, there is no standard protocols , personal preference and individual experience are the guide for treatment. Resource deficiencies and lack of standard less expensive protocols are the great challenges for pediatric oncologists.

Efforts are being made to standardize the level of care being provided in the continent . A protocol for the management of Burkit lymphoma in areas with limited resources is established and sponsored by the SIOP . A lot of work still needs to be done, however.

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ACUTE PROMYELOCYTIC LEUKEMIA. TREATMENT RESULTS WITH TWO CONSECUTIVE BFM PROTOCOLS

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Since Dec/83 to Dec/96 have entered in two consecutive protocols, AML-83 and AML-90 (type BFM), 323 patients (pts) < 15 years with diagnosis of Acute Myeloblastic Leukemia (AML). Thirty two (10%) pts were classified FAB M3 subgroup-Acute Promyelocytic Leukemia-(APL); 13/157 (8.3%) and 19/143 (13.3%) entered in AML-83 and AML-90 Protocols, respectively.Material y methods. For the analysis, we have compared the patients with APL -Group A- vs other FAB subgroups -Group B-.The characteristics at diagnosis were : Group A (M3) 32 pts, Sex (M/F) 18/14, Median Age 9 years (Range 1-15), WBC 4.6xmm3 (0.1-194) and Platelets 13.5/mm3 (0-180); Group B (Others) 291 pts, Sex (M/F) 171/120, Age 6 years (0-15), WBC 13.9 (0.5-690) and Platelets 28. (0-571). Protocol AML-83 consisted 1) induction regimen with VCR+ADR+ARAC+PRED+6MP; 2) Consolidation with CFM+ARAC+6MP; 3) Maintenance therapy with daily 6MP and ARAC in monthly pulses plus ADR bimonthly pulses. CNS prevention was administered with Arac+DMT. Protocol AML-90 included 1) Induction regimen with ARAC+IDR+VP16; 2) Consolidation phase over 6 weeks with 6 different drugs :PRED+6MP+VCR+ADR+ARAC+CFM; 3) Two intensification courses with high-dose ARAC+VP16 and 4)Maintenance therapy with daily 6MP and ARAC in monthly pulses for 18 months. CNS prophylaxis was administered with IT ARAC+DMT. Causes of death during induction treatment (DOI) Group A : hemorrhage-CIV 83% and sepsis 17% vs Group B : sepsis 61 % and hemorrhage-CIV 32% . Results :

Groups	#Pts	#CR (%)	NR	#DOI (%)	EFS 60 mo		S 60 mo	
A (M3)	32	22 (69)	4	6 (!9)	25%	p=0.849	26%	p=0.784
B (Others)	291	200 (69)	35	56 (19)	26%		27%	

Conclusions : 1. APL achieve CR, using BFM type protocols, equal to other AML subtypes , 2) The percentage of DOI was higher than (19%) original BFM protocols, must be improved, 3) The EFS and S were not statistically different between both groups.

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A SURVEY OF PEDIATRIC NON-HODGKIN'S LYMPHOMA

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From January 1990 to December 1995, 47 NHL cases (35 boys, 12 girls, M/F:2.9, 1,5-16 year, median 7 year-old) were admitted to our Center. Histologic features were38% lymphoblastic, 29.7 % Burkitt, 27% non-Burkitt and only 4.2% Large cell. Majority of the cases were in advanced stage on admittion (25.5% in Stage I-II, 73% in stage III-IV). The most common site of involvement was mediastinum and peripheric lymph nodes in lymphoblastic NHL, abdomen in B-cell NHL, peripheric lymph nodes, skin and mediastinum in Large-cell NHL. Incidence of jaw involvement in Burkitt lymphoma was 26% (4/15). Between January 1990-July 1992, COMP and LSA_2L_2 protocols then BFM-90 protocol was applied with a dose modification of HDMTX (from $5g/m^2$ to $1g/m^2$) after two early deaths due to high dose MTX toxicity. A patient with Large cell lymphoma underwent ABMT in 3rd complete remission. Also a patient with disseminated B-cell NHL involving the heart, underwent a successful ABMT in partial remission. A total of six patients who either abondened therapy early or died with complication of diagnostic thoracotomy were uneligable. Remission rate was 87.8% (36/41). Seven patients relapsed. Deaths of B-cell NHL cases were all early (1-8 months), and due to tumor-lysis and acute renal failure (n:3), infection (n:2), HDMTX toxicity (n:2) and relapse (n:1). In lymphoblastic NHL cases, deaths (n:4) were late (11-25 months) and mainly due to infections during resistant relapses. 31.5% (13/41) of all patients died. OS of 41 eligible patients was 69%, RFS 65.5% at five years. RFS of stage I and II was 100% in every histology whereas 58.8% in stage III and 41.67% in stage IV. RFS of Lymphoblastic NHL was 71% at three years, Burkitt 66% and non-Burkitt 70% at four years. One of two Large-cell NHL is surviving. Bone marrow involvement ($p<0.0091$), tumor lysis syndrome ($p<0.00128$), advanced stage (III-IV)($p<0.00128$) and serum LDH>500 U/L ($p<0.0047$) were characteristics associating poor prognosis. As the patients were not randomised and the numbers in different groups are small, comparison of LSA_2L_2 /BFM-86 and BFM-90 protocols for lenfoblastic NHL is not possible. As a conclusion in our series, advanced stage NHL's still have a high mortality but BFM-86 and BFM-90 protocols are feasible in less developed coutries. We hope to achieve better survival rates as supportive care measures improve.

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HODGKIN'S DISEASE IN CHILDREN: 13 YEARS OF EXPERIENCE AT EGE UNIVERSITY

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From 1982 to 1995, 54 patients (median age 9 years, range 2-16 years) were diagnosed with Hodgkin's disease at the Pediatric Oncology Department of the Medical School of Ege University. The sex (M/F) ratio was 2.6/1. Lymphadenopathy was the commonest mode of presentation with cervical nodes being enlarged most often (85%). Histologic patterns were classified as mixed cellularity 29, nodular sclerosis 16, lymphocyte predominance 9. Clinical stage at presentation was: Stage I in 13 patients, Stage II in 19, Stage III in 14 and Stage IV in 8. "B" symptoms appeared in 44%. Staging laparotomies and splenectomies were performed in 14 cases. Seven patients had a higher pathological stage than clinical stage. Before 1989, all patients received only chemotherapy (6 cycles of MOPP, COPP or ABVD), whereas after 1989, the patients received chemotherapy plus radiotherapy. The patients were treated with MOPP, COPP or ABVD (3 cycles) before irradiation in early stages or before and after irradiation in advanced stages. The five years overall and relapse-free survival were 91.7% and 77.6%, respectively.

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NITROGEN MUSTARD OR NO NITROGEN MUSTARD IN PEDIATRIC HODGKIN'S DISEASE : A QUESTION TO BE ANSWERED

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MOPP regimen (Nitrogen Mustard, Vincristine, Procarbazine Prednisolon) has a proven effect on out come in Hodgkın's Disease but Nitrogen mustard increases morbidity causing high rates of sterility, so Nitrogen Mustard (-) regimens are preferred all over the world as well as in our unit.

41 Hodgkin's Disease patients treated with MOPP regimen are compared with those 36 Hodgkin's Disease patients who were treated with Nitrogen Mustard (-) regimens. Nitrogen Mustard (-) regimens were COPP (14 patients) and COPP + OPPA (22 patients) in which Cyclophosphamide or Adriamycin were used instead of Nitrogen Mustard.

Overall survival rates and mean follow up were 89.2% and 75 months (l-l60 months) for MOPP regimen; 97.3% and 68 months (5 -180 months) for COPP regimen; finally l00% and 20 months (5-39 months) for OPPA+COPP regimen with no statistically difference ($P = 0.5$) as relapse free survival rates were 65%, 70.5%, 81.8% for MOPP, COPP, COPP+OPPA respectively ($p = 0,44$).

As a conclusion N. mustard (-) regimens in Hodgkin's disease have no significant difference with N.mustard (+) regimens, but multicenter studies with high number of patients are needed to evaluate the proposed regimen for both morbidity and mortality.

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A TWENTY-ONE YEAR EXPERIENCE WITH 120 WILMS' TUMOR CASES

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A retrospective study was conducted on 120 children with Wilms' tumor who were admitted to Istanbul University, Istanbul School of Medicine, Department of Pediatric Hematology / Oncology between 1975-1996. There were 74 boys and 46 girls with a mean age of 2,58±1,75 years (4 months - 15 years). The patients were admitted with the complaints of abdominal mass (67%), hematuria (16%), abdominal pain (14%) and weight loss (8%). The cases with massive tumoral mass or involvement of vital structures received preoperative chemotherapy or radiotherapy. Ninety-four of the cases underwent primary surgical intervention. Thirty-five percent of the cases had the tumor in the right kidney, 60% in the left and 5% had bilateral origin. Four cases with pulmonary and 2 cases with hepatic metastasis required sugical resection following postoperative chemotherapy and radiotherapy. The extend of the disease was classified as stage I (7%), stage II (27%), stage III (25%), stage IV (36%) and stage V (5%). All patients received chemotherapy consisting of Vincristine + Actinomycin-D ± Adriamycin ± Cyclophosphamide ± RT according to their clinical stages and pathology for 26-65 weeks. We had to perform 11 second look and one third look laparotomies in order to evaluate the results of the therapy and to resect any remnant that was observed.

The five year overall survival rate is found to be 71%. According to stages the five year survival is found to be 100% in stage I, 93% in stage II, 90% in stage III, 52% in stage IV, 12% in stage V.

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HEPATOBLASTOMA IN CHILDREN : ISTANBUL EXPERIENCE

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Between 1984-1996, 16 children (10 M, 6F) who were diagnosed and treated for hepatoblastoma in our center were evaluated retrospectively.The median age was 16 months (3mo-9 year) of whom 75% were < 3 years of age. The most frequent presenting symptom was abdominal distention/mass (87.5%);pallor was found 25%, fever 25%, weight loss 18.7% ,icterus 6 % of the patients. 12.5 % of the patients were in stage I, 43.7% in stage II, 31.3% in stage III, 12.5 % in stage IV.In 56.2% of the patients the tumour was localizated at the right lobe and the remaining patients had the tumour at both lobes of the liver.All patients had a high alpha fetoprotein levels. Histopathological types were epitelial in 68.7% and mixed in 31.3 % of the patients..Primary total tumor resection could be possible in 7/16 (43.7%) of the pts.(in 3 pts with no residual tm,in 4 pts with microscopic residual tm).Wedge biopsy or partial resection was applied in 9 patients.6/16 patients (37.5%) were died, because of preop.emboli (n:1),post op.sepsis and DIC (n:3) ,fulminant hepatic failure (n:2) perioperatively before the administration of chemotherapy. 10/16 patients (62.5%) could receive chemotherapy and 7/10 (43.7%) succumbed to death because of progressive disease (n:5) , chemotherapy related complications (n:2). 2 patients with no resectable tm at presentation became resectable after chemotherapy.2/16 pateints were lost to follow up. 1/16 patient is alive and well for 8 months. As a result 13/16 patients (81.2%) died and 2 year overall survival and DFS were found 33% and 17% respectively. Because of high perioperative deaths in the centers where postop care is insufficient, we recommend preoperative combination effects during L-asparaginase treatment, but allergic reactions were found in 2 children of BFM group and in 10 children of MB group ($p<0.03$). The more detailed analysis of protocols, including the comparison of different phases of intensive treatment will be presented.

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COMPARATIVE STUDY OF TOXICITY OF TWO PROTOCOLS FOR TREATMENT OF CHILDHOOD ALL - BFM-90M AND MB-91 IN MOSCOW.

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In randomized multicenter trial in Russia modified protocol BFM-90 (BFM-90m) and original protocol Moscow-Berlin (MB-91) were shown to have no difference in effectivity of treatment according to the CR, relapse rate and mortality (reported on SIOP, Vienna, 1996). The purpose of present study was to compare the toxicity of the intensive phases of therapy by two protocols - BFM-90m MB-91 according to hematological parameters, blood biochemistry data, the cases of transfusions and the frequence of inpatient care. 104 patients with ALL were randomized in two Moscow clinics from December 1992 to September 1995 and 94 patients were enrolled in comparative analysis of toxicity (48-BFM 90m, 46 -MB 91). The patients receiving MB-91 protocol were demonstrated to have less requirements for blood transfusions (mediana was 5 for BFM-90m vs 2 for MB-91, $p<0.00001$) and equal requirements for platelets transfusions (mediana was 1 for both protocols). Number of patients with episodes of agranulocytosis longer then 10 days was significantly less in protocol MB-91 vs BFM-90m ($p<0.04$), but there were no differences in frequency of infections during intensive therapy. Duration of hospital care was 41.5 days in BFM-group and 23 days in MB-groupe ($p<0.001$). There were no statististical difference in frequency of nausea/vomiting and gastrointestinal adverse

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TREATMENT OF NON-HODGKIN'S LYMPHOMA(NHL) IN CHINESE CHILDREN, 1978-1992

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Fifty-six children ages <12 years were diagnosed histologically as NHL between 1978 to June 1992 and treated with two treatment protocols in our hospital. Murphy classification of staging was utilized. Four(7%) had Stage II disease, 18 (32%) Stage III, and 34 (61%) had stage IV. Bone marrow with > 25% tumor cells were seen in 26 (46%) CNS was involved in 5 (9%). The proportion of staging groups was similar in the two treatment groups. Twenty-seven patients diagnosed between 1976 and 1982 (Group 1)were treated with COMP or COPP without CNS prophylaxis. Their initial CR rate was 46% (10/29), with a 4 year event free survival (EVS) of 11% (3/27). Those treated after 1982 received Pro-MACE-MOPP. Intrathecal (IT) DX, MTX, Ara-C were given q 2 weeks x 6 to the first 13 patients, and q week x 8, then q 2-3 months for two years to the last 16 patients. The initial CR rate in Group 2 patients was 90% (26/29) and the 4 year EFS was 34% (10/29). A CNS relapse occurred in 4 of the first 13 Group 2 patients, while there was only 1 relapse in the last 16 patients. No patient with CNS relapse survived in either Group. **Conclusion:** Pro-MACE-MOPP therapy is superior to that of COMP or COPP for Stage II-IV Non-hodgkin's disease, and intensive IT therapy can protect the CNS from infiltration.

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THE RESULTS OF CHEMOTHERAPY (CT), HYPERFRACTIONATED RADIOTHERAPY (RT) OR SURGERY (S) IN NON METASTATIC EWING SARCOMA

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From 01.91 to 12.95, 15 children with non-metastatic Ewing sarcoma (ES) were treated with a protocol consisting of 52 weeks (wks) of CT of alternating VAC-A (vincristine, actinomycin D, cyclophosphamide, adriamycin) and IE (ifosfamide, etoposide). After 6 wks. of induction CT, patients were evaluated on 9th wk. for local therapy (RT or S). Male/female ratio was 9/6 and median age 8.5 years (4.5-16). The tumor locations were extremity in 7 cases, iliac wing in 3 cases and others in 5 cases (clavicule, rib, vertebra, foot), and the size of tumor was ≤ 10 cm only in 6 cases. After induction CT,

radiological objective response in soft tissue mass observed on computerized tomography and NMR was obtained in 10 patients (6 cases with partial response and 4 cases with complete response). As local therapy S was used in 5 and RT in 10 cases. The dose of hyperfractionated RT (5040-6240 cGy; 120 cGyx2 fr./day) was adjusted according to the response obtained by induction CT. Median survival was 22 months (11-55) and the actuarial survival was 71% in 2 years. Local relapse was seen only in 2 cases. In conclusion the results of this study show that this protocol is safe and effective in the treatment of non metastatic ES, especially when the dose of RT is adjusted according to the radiological response obtained after induction CT.

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RETROSPECTIVE ANALYSIS OF 44 CHILDREN WITH RETINOBLASTOMA

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The survival of patients with retinoblastoma (Rb) has gradually improved over the last decades. The early diagnosis and the improved therapy succeeded to assure a cure - rate of more than 90%. In order to find out the origin of our poor results we reviewed the charts of 44 children with Rb from our observation in the period of 1978-1997. We correlated the evolution with the clinical, tomographic, ultrasonographic and histopathological data and also with the treatment modalities. 33 had an unilateral, 10 a bilateral and 1 a trilateral Rb; 4 were withhereditary and 40 with sporadic form. The diagnosis was done at a mean age of 2.8 years and classified as a Reese - Ellsworth group 4 in 9 and 5 in 35 patients. The histopathological examination revealed in 32 choroidal, in 28 optic nerve and in 12 patients an orbital invasion. At the time of diagnosis 4 had neurological involvement or bone marrow metastases. The treatment consisted of: enuclation - 42, enuclation + radiotherapy -4 and enuclation + chemotherapy - 9 patients; the therapy was refused in 2 cases. The five year survival was 27.5%. The correlative analysis pointed out the unfavourable predictive value ($p < 0.001$) of the bilateral and trilateral Rb, of the orbital, choroidal and optic nerve invasion, of the Rb with metastases. The absence of an appropiate radiotherapy seems to be of decisive importance.

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IS IT NECESSARY TO DEVELOP SPECIFIC THERAPEUTIC APPROACHES FOR MIDDLE EAST PAEDIATRIC LYMPHOMAS? (PAEDIATRIC LYMPHOMAS IN KUWAIT CANCER CONTROL CENTRE [KCCC] 1995-1996).

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Kuwait Cancer Control Centre.

The specificity of Middle East lymphomas use to be emphasized with requirements to develop specific therapeutic approaches for them. In 1995 the paediatric oncology programme has been upgraded in KCCC and recent international paediatric oncology protocols have been adopted in order to confirm their feasibility and effectivity in the Middle East conditions.

For Hodgkin's disease HOD 90 from Stanford University USA, and for NHL, BFM 90 were standard therapeutic protocols for children with lymphomas treated in KCCC in 1995 and 1996. During the period April 95 - February 97, twenty six paediatric lymphomas have been diagnosed and treated in our institution - 16 HD and 10 NHL.

Age 3-16 years (median 9.2), 16 boys and 10 girls.
FU (10-23) months, median FU 16.7 months.

Stage	LP	NS	MC	LD	Non B NHL (TdT+)	B-NHL (TdT-)	LCAL
I	1	1	-	-	-	-	-
II	1	1	1	-	-	-	-
III	-	5	4	-	4	5	-
IV	-	1	1	-	-	-	-

All these patients have achieved CR. In HD group all patients are maintaining 1. CCR so far (EFS + OS 100%). In NHL group there is one early relapse (abdominal stage III Burkitt's NHL with LDH 235 U/L only at presentation (EFS for NHL 90%, OS 100%).

Despite low number of patients and short follow up our results suggest that these widely used protocols are highly effective and feasible in the Middle East conditions and so far there is no evidence to support the necessity of developing local specific protocols.

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NON-HODGKINS LYMPHOMA (NHL) IN CHILDREN. CLINICAL PRESENTATION

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Between 1/81 and 12/94, 290 previously untreated children under 15 years of age with NHL were diagnosed at the Department of Pediatrics of the INEN.
185 were males (64%) with a M/F of 1.76; the median age was 6 yrs with a range of 5 months to 14 yrs. The most common primary site was intra abdominal, 38% (110/290) followed by peripheral nodal, 20% (59/290); head and neck, 14% (41/290); mediastinum, 13% (39/290); subcutaneous, 9% (26/290), and miscellaneous, 5% (15/290).
The most frequent histology according to Rappaport was undifferentiated, 30% (110/290), followed by lymphoblastic, 20% (58/290); histiocytic, 19% (56/290); lymphocytic, 11% (33/290); mixed, 2% (7/290); Ki 1, 2% (7/290); others, 2% (6/290), and unclassified, 5% (13/290).
The stages according to Wollner were, I: 1% (4/290); II: 21% (61/290); III: 46% (132/290); IV: 32% (93/290). In the stage IV group, 9 (9.6%) presented with CNS involvement and 84 (90.3%) had bone marrow involvement. Of the latter, 14 (16.6%) had less than 25% blasts; and 70 (83.3%), more than 25% blasts in the marrow.
All patients with early stage disease were treated with CVP +/- involved field radiation 2,000 cGy, and those with stage III and IV received the LSA2L2 +/- RT to the primary site except the primary intra abdominal cases. The disease-free survival for the entire group is 65% with a median follow-up of 8 years.
This aggressive disease is curable with treatments like the ones used when intensive measures are taken to prevent tumor lysis, infections and metabolic complications.

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PRIMARY SUBCUTANEOUS NON-HODGKINS LYMPHOMA (NHL) IN CHILDREN.

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Between 1/81 and 12/94, 290 previously untreated children under 15 years of age with NHL were diagnosed at the

Department of Pediatrics, INEN. 26 (9%) presented with primary subcutaneous tissue involvement.
14 (54%) were females with an F/M ratio of 1.17, with a median age of 7 years (range 5 monts to 14 yrs). The most common histology was lymphocytic, 38% (10/26); undifferentiated, 15% (4/26); histiocytic, 11% (3/26); lymphoblastic, mixed, Ki 1 and unclassified, 8% each (2/26), and one case with peripheral T cell NHL.
The stages were: I, 1 (4%); II, 10 (38%); III, 3 (11%); IV, 12 (46%). 88.5% of the patients (23/26) presented with subcutaneous involvement of the tissues in the face or scalp, and the remaining 3 (11.5%) with lesions in the extremities. The involvement ranged from 2 to 12 cm in size. In the patients with stage IV disease, 2 (16%) had initial involvement and 10 (83%) had diffused infiltration, one of which also had CNS involvement.
The disease-free survival for this group of patients is 58%, with a median survival of 8 years.
One of the problems of this type of presentation is the delay in recognizing and making an accurate diagnosis of the soft tissue tumor. Thus, 46% of our patients already had bone marrow involvement at the time of admission to the INEN.

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Therapeutic results of the treatment of children with Hodgkin lymphoma according to DAL HD-82

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Objective: To evaluate the efficacy of DAL HD-82 for the treatment of Hodgkin lymphoma in childhood. The aim of the protocol is a reduction in the chemotherapy and irradiation without subsequent compromise of the event-free survival /EFS/.
Forty children with histologically proven Hodgkin lymphoma, age 2,5 to 17 years have been treated at the Oncohaematological ward in Plovdiv for a period of 13 years /from 1983 to 1996/ according to DAL HD-82 protocol. Eight of them have been in I clinical stage, 18-in II, 9-in III and 5-in IV. According to the protocol requirements the patients have been stratified in 3 risk groups, concerning the duration of chemotherapy, which have been followed only by involved field irradiation with a dose range of 25 to 35 Gy. In two of the children in I clinical stage irradiation have been substituted for two additional COPP cycles because of the small age. 5-years EFS in the studied group is 92,5% regardless of the clinical stage; there is a loss of follow-up in 2 patients in IV clinical stage and a relapse of the lymphoma in one child with inadequate initial treatment.
In conclusion DAL HD-82 is a highly effective protocol, easy to be carried out on a outpatient basis without severe myelosuppression and secondary infectious complications. In the studied group no serious long-term sequelae of the combined chemotherapy and irradiation have occured so far.

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"SURVIVING CHILDHOOD CANCER: ALL IS WELL THAT ENDS WELL!?" - AN INFORMATION BOOKLET FOR PARENTS AFTER TREATMENT ENDS

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Childhood cancer has late psychosocial consequences for the whole family: former patients, parents, and siblings. The complexity, seriousness, and duration of these consequences underline the need to address them. Educating the family about the late psychosocial consequences can be an effective way to support them in coming to terms with the disease. Most children are of young age when their treatment is ended and therefore educating parents is most effective to prevent or alleviate late psychosocial consequences.

The booklet *Surviving childhood cancer: All is well that ends well!?* is written for parents whose child has completed treatment. The booklet provides information about the late psychosocial consequences of childhood cancer and aims to stimulate discussions within the family as well as with the medical and psychosocial staff at the clinic. The contents are in three sections. The first two sections discuss the former patient's and sibling's experiences with the disease and how parents can help the patient and sibling coming to terms with their experiences. The last section provides insight into the coping process of the individual parent and addresses differences in coping styles between partners.

We performed a pilot study to the readability and contents of the booklet. In total, 43 parents (16 fathers and 27 mothers) responded. All parents indicated that the booklet was easy to read. The late psychosocial consequences as described in the booklet were recognized by 91% of the parents. Seventy percent reported that the booklet had provided more insight into their situation. The majority of parents indicated that the information was useful in dealing with the former patient (60%), the sibling (73%), the partner (67%), and themselves (67%). Seventy percent of the parents felt supported by the booklet and 76% reported that the booklet contributed to a better understanding of their problems by the social environment such as extended family, school, and friends.

We conclude that information on the late psychosocial consequences of childhood cancer is appreciated by parents and support them in coping with the late consequences of childhood cancer. The results of the pilot study are being used for the final version of the booklet in the Dutch and English language.

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SUPPORTIVE TALK-GROUPS FOR SIBLINGS OF CHILDREN WITH CANCER.

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A life-threatening illness like childhood cancer is an emotional experience for all the family members involved. With an average age of onset of 3 to 4 years and treatment lasting 2 to 3 years, childhood cancer affects the family system during its early child-rearing years. Siblings experience several distresses: change of interaction with the family, a feeling of displacement, concern of own health status, feeling responsible for the cancer, wanting to trade places with the patient, fearing the patient would die, and feelings of jealousy.
The psychological team of our Pediatric Psychosocial Department has frequently been consulted for problems of siblings of pediatric oncology patients. This resulted in the initiation of supportive talk-groups for siblings of children with cancer. Until now several groups with children between 8-12 years have come together. The supportive group takes five sessions. Most reported problems described by the parents were school functioning, troublesome behavior and feelings of sadness of the sibling. During the support groups several topics are discussed with the children: knowledge about the disease and questions they have about it, reactions of other children in school such as teasing and possible strategies toward teasing at school. During

every session one of the children shows pictures of his or her ill sibling. This gives the opportunity to generate topics for discussion. Every support group is ended with a conducted tour on the pediatric oncology ward. Generally, siblings and parents are positive about the supportive groups. This will be illustrated with empirical evidence.
In two groups anxiety levels were measured before and after the sessions, and qualitative data was analyzed as well. Anxiety levels decreased after participation in the groups. This was confirmed by judgements by psychologists of evaluation interviews. These support groups emphasise the need for more information about which siblings are especially at risk and are in need of special attention.

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COPING OF PARENTS AND SIBLINGS WITH THE DEATH OF A CHILD WITH CANCER AFTER TERMINAL CARE

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Patients and Methods: One hundred pediatric patients with cancer treated at the Hospital for Children and Adolescents, University of Helsinki, Finland, died during 1987-92. Seventy children died while in terminal care. The underlying diseases were brain tumors (21), other solid tumors (24), and leukemias (25). The method of evaluation was a structured interview of every parent separately.
Results: Parents of 60/70 children were interviewed; they were 55 mothers and 49 fathers (44 couples). Almost half (44%) of the parents felt that the death of their child did not have any remarkable influence on their interrelationship; 32% felt they got closer, and only 24% felt that this event drifted them apart. Four couples divorced after the death. Most parents did not have any physical or mental problems. A serious problem with alcohol was revealed in 8%. One-forth of the parents returned to work within one month after the death; the fathers did so earlier than the mothers. 48/60 children had 77 siblings aged 0.2-27 years. One-third of the parents had been overprotective and two-thirds had reacted normally, according to their own judgement. In the parents´ opinion, 84% of siblings did not have any kinds of problems. 16% had fears, behavioral problems, problems with their friends, or school-related problems. For more than half of the families help was offered either by the personnel of the oncologic unit (42%) or by other instances such as the church (12%), but only few families used extra help. The main ways for coping and recovering were time, work, and support from relatives and friends. According to the parents´ own opinion, the recovery took 1-1.5 years, being shortest in the leukemia group. In one-third of the families a new baby has been born.
Conclusion: We feel that most of the parents and siblings have potential and capability to recover normally after the death of a child, although they will never be the same as before.

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INTERDISCIPLINARY COLLABORATION IN PEDIATRIC ONCOLOGY: THE PHYSICIAN / NURSE / PARENT-SHORT-QUESTIONNAIRE (PNP-SQ) OF FAMILIAL ADHERENCE IN INPATIENT CARE

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Objective: In pediatric oncology the different professional groups work close together with the families. For high quality health care it is required to structure the interdisciplinary collaboration between psychosocial, medical and nursing team and the families. The PNP-SQ serves to optimize this collaboration during the course of therapy.
Method: The PNP-SQ is presented to the physician, nurse and parents of all patients at three points of time. The PNP-SQ contains 18 items about the adherence of parents and children with a 4-point-rating-scale (0-3). The data in the PNP-SQ of 26 families within the first two months of therapy were compared with the psychological ICD-10-diagnoses (familial risk factors) and with the parental coping assessed in the FKV (Freiburger Frageb. Krankheitsverarbeitung).
Results: In the PNP-SQ there are comparable high assessments of the familial adherence from physicians (1.99), nurses (2.18) and parents (2.08). On item level we found considerable differences in the assessments of the staff and the parents (e.g. information seeking, cooperation, emotional state). Low-risk-families in ICD-10-diagnosis and parents with positive coping were in general assessed as better cooperating and in better emotional state than high-risk-families and those with unfavourable coping styles.
Conclusions: The PNP-SQ is a useful instrument for the assessment of the adherence of parents and children during therapy. The assessments of the physicians, nurses and parents form the basis of a successful collaboration. The psychological ICD-10-diagnosis and the parental coping at beginning of therapy are of high prognostic value so that specific psychological interventions will be possible at early time.

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SCHOOLING OF PEDIATRIC CANCER PATIENTS - THE VIENNESE SINGLE CASE CARE APPROACH

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In addition to their threatening illness, patients lose contact to their familiar environment as they are not allowed to attend school during the intensive treatment by chemotherapy. In order to compensate for that loss, a co-operative project between school authorities and St.Anna's Children's Hospital has been established in Vienna. Throughout one school year, six teachers, who are employed and paid by the Vienna Board of Education, look after 30 children aged 6-18.One teacher is responsible for two or three children at a time, permanently staying in contact all through the course of treatment, teaching at home or in hospital, the patients' condition permitting. Moreover, the teacher is confronted with the emotional and social impact of the illness on the family, thus holding a confidential position caring for child and family. The project provides the patient with a future perspective throughout the illness. Academic requirements and standards for the children are not lowered, which keeps them in touch with reality and gives them a sense of achievement. The teachers' task is to ensure permanent contact between children and their school, on a formal level as well as on an informal one, thus preparing a smooth reintegration after the illness. Co-operation with hospital staff is guaranteed, since the psychosocial team, consisting of psychologists, kindergarten nurses, teachers and a chaplain, meets once a week to exchange information. The project was established in 1985 and has since then made a successful re-entry into school possible for 75% of our pupils/patients.

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EVALUATION OF THE SAFETY AND COST EFFECTIVENESS OF PEDIATRIC DOSAGES OF G-CSF IN PRE-FILLED SYRINGES.

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G-CSF (Filgrastim) can be used to shorten the period of neutropenia ($<0.5x10^9/l$) in children treated with high doses of cytostatics. The prescribed dosages (5 μg/kg/day for a maximum of 10 days) were prepared daily at home by the parents themselves or the district nurse and given subcutaneously. Because no preservative is present in the vials, it is recommended to use a vial only once and thus, in children, the nonused portion has to be discarded. This is an expensive waste. We investigated the feasibility, bacteriological safety (up to 7 days) and economic outcome of dispensing pediatric dosages of filgrastim in pre-filled syringes by community pharmacy's.

Methods. The hospital pharmacy prepared a protocol in which we asked the community pharmacists to aseptically draw the prescribed dose into tuberculin syringes and dispense to the patient for a maximum period of 7 days. The parents were asked to fill in a questionnaire about their experiences. The community pharmacists were asked how many vials of G-CSF were used.

Results. From July 1996 till February 1997 9 patients are treated with G-CSF in 40 courses. Their weight was 8-32 kg. We received 40 syringes for bacteriological culture. 39 were sterile, 1 proved to be contaminated with *Staph. epidermidis*. This syringe was not kept under the prescribed circumstances and brought to the hospital in an unhygienic way. The parents highly preferred pre-filled syringes. They experienced much less uncertainty about dosing and hygiene. For all courses 48 vials of 300 μg and 7 vials of 480 μg were used at a total price of DFl. 14.754,91. In the old way 207 vials of 300 μg would have been used at a total price of DFl. 51.592,68. This means a saving of DFl. 36.837,77 (71%) has been achieved.

Conclusion. It is bacteriologically safe to pre-fill syringes of G-CSF in this way. Parents highly prefer this procedure. For pediatric dosages the cost saving is substantial.

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PROTEIN-ENERGY MALNUTRITION AND SKELETAL MUSCLE WASTING IN CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA

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Since malnutrition is a common problem in children in developing countries, we prospectively assessed the nutritional status of patients with ALL at presentation. The changes in body weight and the amount of skeletal muscle wasting after remission-induction chemotherapy was also determined. Somatometric measurements and ultrasonographic evaluation of skeletal muscle and subcutaneous fat were done in 18 children with ALL. Malnutrition was evident in 11 cases (61%) at diagnosis. In 6 patients, the malnutrition could be designated as acute. Induction chemotherapy led to a decrease in weight in 6 patients (range 0.2 to 5.8 kg), who had a complicated course. These cases also demonstrated skeletal muscle wasting. The decrease in mid-arm muscle circumference ranged from 0.04 to 3.30mm whilst the quadriceps muscle thickness decreased by 0.4-2.0mm. Subcutaneous fat increased in all. The study draws attention to the fact that malnutrition exists in 60% of children with ALL probably as a consequence of the disease, delayed referrals/diagnosis and the prevalence of poor nutrition in the community. The findings highlight the need for evaluating the role of nutritional supplementation and the interplay between malnutrition and pharmacokinetics of chemotherapeutic drugs.

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HOME THERAPY (HT) IN PEDIATRIC ONCOLOGY : RESULTS IN GENEVA.

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In Geneva, home therapy (HT) is well developed for adult patients while pediatric cancer patients are presently treated with hospitalizations and/or outpatient visits. To re-orient care towards a home setting, and to minimize hospital exposure, we cooperated with two private home care agencies[2,3] in the development of pediatric home treatments previously administered in the hospital. Since January 1996, we have organized 16 HT in 11 children with cancer, aged 7.3 years (3.8-14.2) whose parents were willing to participate to HT. Treatments through central venous catheters consisted of iv antibiotics (8), iv hydration before and/or after chemotherapy (5), iv analgesics (2) and parenteral nutrition (1) ; no iv chemotherapy was given at home. Median duration of HT was 3 days (1-45). During the study period, no emergency hospitalization or indesirable incident occurred. One child was hospitalized because of declining general condition unrelated to HT. Home therapy avoided 125 hospitalization days ; the mean cost of the first 11 HT was equivalent to 310 US$/day (175 to 762 $) with a global saving of 56000 $. The following charges/day of HT for the family and the insurance company are detailed below (11 first HT). These charges are compared with those of the same treatments given during hospitalization :

	Family Charges	*Insurance Charges*	*Real costs*
Hospitalization	AC	197 $	758 $*
HT	10%**	310 $***	310 $

AC : accessory costs (food, travels and loadging). * : Mean cost of one hospitalization day in 1996. ** : to a maximum of 206 $/year. *** : drugs and supplies (40%), home nurses (38%) et outpatient hospital costs (22%).

The families and children were fully satisfied by HT although the required parenteral presence 24H a day at the child's side was demanding. HT is feasible for selected families and economically advantageous provided that nurses and doctors are available 24 hours a day.

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Dactinomycin associated Veno-occlusive Disease of the Liver, successfully Treated With Prostaglandines.

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Veno-occlusive disease (VOD) is a well-known entity with important mortality in children receiving a BMT. Chemotherapy-induced veno-occlusive disease (C-VOD) of the liver is rare. Objective: We report on three children with a solid tumor (fibrosarcoma, nephroblastoma(2)) who experienced a severe hepatic VOD, after treatment with regimens containing dactinomycin (ACT) according to standard SIOP protocols. Within the first 10 weeks of treatment, the children suffered from pain in the right hypochondrium, fever and irritability. Symptoms rapidly worsened with lethargy, pallor, hepatomegaly and ascites, accompanied by a refractory trombocytopenia, coagulation dysfunction and a rapid increase of liver enzymes (several thousands U/L). Hepatic VOD was strongly suspected and continous IV administration of prostaglandin E1 (PROSTIN) at a dose of 0.6 μg/kg/hour was started, which resulted in a significant improvement of both clinical and laboratory findings within 48 hours. This treatment was well tolerated, all three children recovered from their hepatic insult. A liver biopsy, performed in 2, confirmed the diagnosis of VOD. Besides chemotherapy, isoflurane anesthesia used for placement of a central catheter in 1 and abdominal irradiation for a stage III Wilms' in a second patient was given.

Conclusion: C-VOD can cause fulminant hepatic failure and urgent recognition is mandatory. Early administration of PGE1, a vasodilatory prostaglandin with antithrombotic activity, significantly improved patients' status within 48 hours.